FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY

CUK-H03449-12-0271585

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

OFFICIAL ORGAN OF
THE AMERICAN ROENTGEN RAY SOCIETY
THE AMERICAN RADIUM SOCIETY

CALCUTTA UNIVERSITY
CENTRAL LIBRARY

TRAIAN LEUCUTIA, Editor
KENNETH L. KRABBENHOFT, Assistant to the Editor
ASSOCIATE EDITORS
HARRY HAUSER RUSSELL H. MORGAN EDWARD B. D. NEUHAUSER
WENDELL G. SCOTT

12

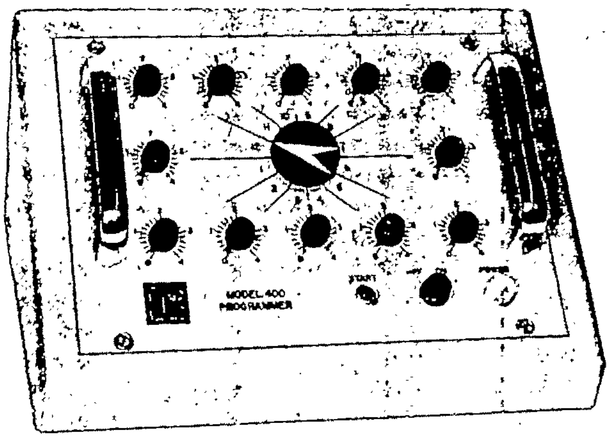
CONSULTING EDITORIAL BOARD
PAUL C. AEBERSOLD
OSCAR V. BATSON
JOHN CAFFEY
ROSS GOLDEN
PAUL C. HODGES
HOWARD B. HUNT
JOHN H. LAWRENCE
REED M. NESBIT
EUGENE P. PENDERGRASS
U. V. PORTMANN
LAURISTON S. TAYLOR
OWEN H. WANGENSTEEN
SHIELDS WARREN

Issued Monthly for the American Roentgen Ray Society by
CHARLES C THOMAS · PUBLISHER · SPRINGFIELD · ILLINOIS

VOLUME 90 OCTOBER, 1963 NUMBER 4

Sixty-fourth Annual Meeting, American Roentgen Ray Society
Queen Elizabeth Hotel, Montreal, Quebec, Canada
October 8-11, 1963
For Preliminary Program see July issue
For Instruction Courses see August issue

PLUG IN EXTRA CONVENIENCE

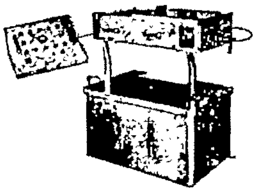


615 · 842305
AM 35

NEW MODEL 400 PROGRAMMER

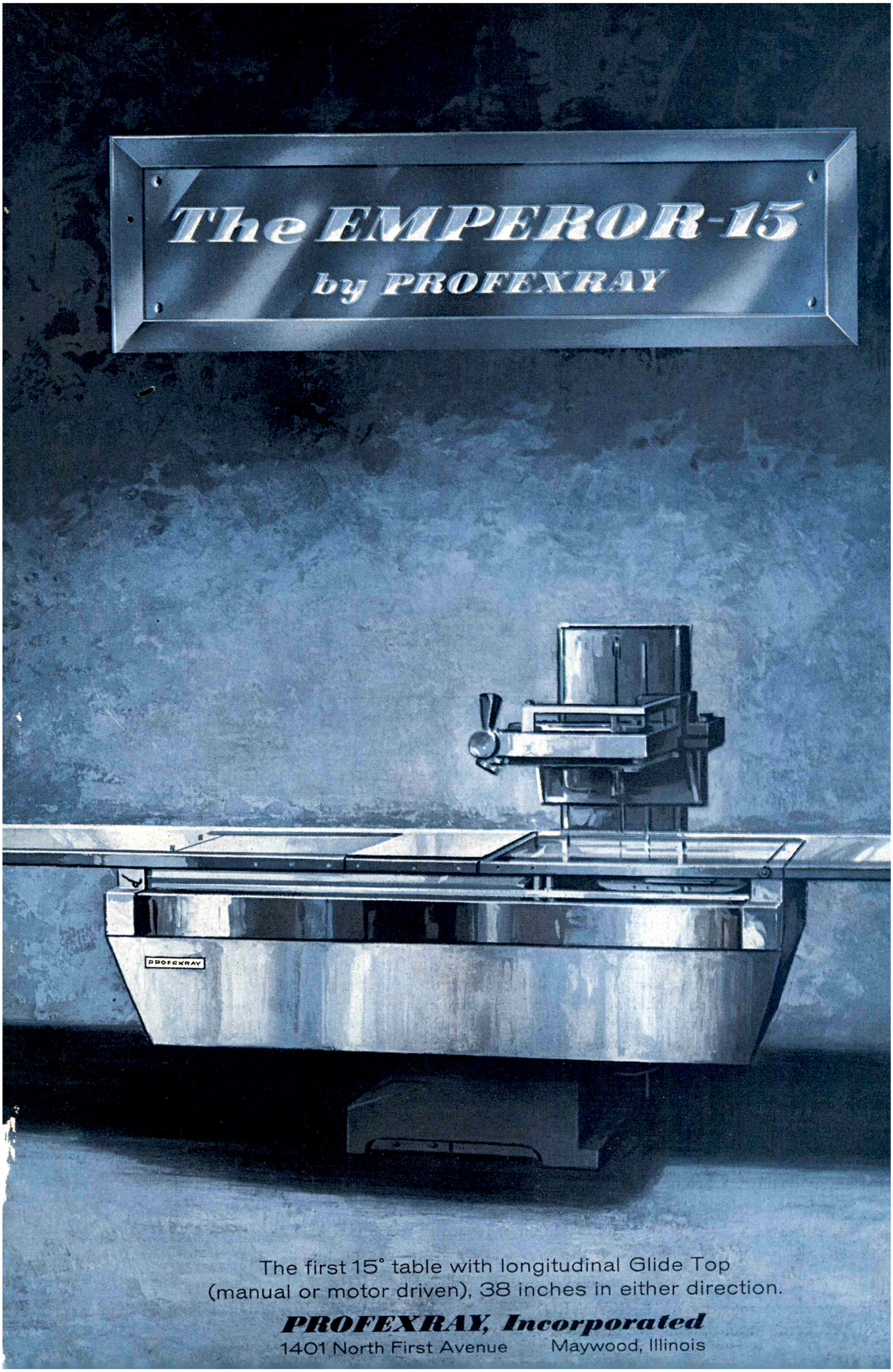
271585

for the Sanchez-Perez Universal Automatic Seriograph. Convenience, an outstanding feature of the Universal Automatic Seriograph, acquires even greater significance with the addition of the Model 400 Programmer. Designed to be plugged into the Seriograph without modification, the Model 400 provides: • Complete series time selection for the high-speed, 12-cassette Automatic Seriograph • Individual time-interval control of each cassette • Preselection — and reselection — of time intervals • Control from remote site • Integral cassette counter • Portability for desk or wall operation • Easy adaptability to automatic dye injectors • Simple adaptability to biplane operation. • Obtain complete information about the convenience-enhancing Model 400 Programmer.



Please address your inquiries to: The Automatic Seriograph Corp., 4900 Calvert Rd., College Park, Maryland. Our telephone number is: UNion 4-5678.

THE AUTOMATIC SERIOGRAPH CORPORATION
A DIVISION OF LITTON INDUSTRIES



The first 15° table with longitudinal Glide Top
(manual or motor driven), 38 inches in either direction.

PROFEXRAY, Incorporated
1401 North First Avenue Maywood, Illinois

GENERAL INFORMATION

Manuscripts offered for publication and other correspondence relating to the editorial management and books for review should be sent to Dr. Traian Leucutia, Editor, 110 Professional Building, Detroit 1, Michigan. Contributions may be sent in foreign languages and will be translated if found acceptable. Original articles are published with the understanding that they are contributed exclusively to The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine.

A certain number of illustrations will be supplied free of cost; but special arrangements must be made with the Editor and Publisher for excess illustrations and elaborate tables.

Fifty reprints are furnished without charge to authors. Additional reprints may be purchased according to a scale of prices that accompanies galley proofs. As soon as each issue is printed, the type is destroyed except for reprint orders *in hand*. Reprint orders *must* be returned with corrected galley proof to the Editorial Office if additional reprints are desired.

Correspondence regarding subscriptions, advertisements, and other business relating to The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine should be addressed to Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois. (All requests to be submitted in writing.)

Manuscripts should be typewritten, with double spacing, and good margins (not on thin paper) and the *original* should be sent to the Editor. The author should keep a carbon copy, as the original is not returned. The name of the author should appear on each sheet of manuscript. Tabular materials should be typed on separate sheets; likewise bibiliographical lists, footnotes, etc.

Drawings and charts for reproduction should be made in black (*never* in blue). Photographic prints of plates or slides on glossy paper produce the best half-tones.

All photographs and drawings intended for illustrations should be numbered, the top plainly indicated, and an abbreviated title of the paper placed on the back of *each one*.

Legends for illustrations should be typewritten in a single list, double spaced, with numbers corresponding to those on the photographs and drawings, instead of attaching each legend to its corresponding figure.

Care in preparation of bibliographies will save much time and correspondence. Each reference in a bibliography should include the following information in order the indicated: Name of the author with initials; title of the article; name of the periodical year, volume and pages. It is requested that the authors use the following as model:

1. Olcott, C. T., and Dooley, S. W. Agenesis of lung of infant. *Am. J. Dis. Child.*, 1943, *65*, 766–780.

The month should be given if the reference is to an issue of the current year. An alphabetical arrangement of the authors is requested.

The author should always place his full address somewhere on his manuscript. This is very important and is often omitted.

For information regarding membership in the American Roentgen Ray Society, address the Chairman of the Executive Council, Dr. J. P. Medelman, 110 Birchwood Avenue, White Bear Lake 10, Minnesota.

For information regarding the program of the annual meeting of the American Roentgen Ray Society, address the President-Elect, Dr. Ralph M. Caulk, 101 Irving Street, N.W., Washington 10, D. C.

For information regarding membership in the American Radium Society, address the Secretary, Dr. Justin J. Stein, U.C.L.A. Medical Center, Los Angeles 24, California.

For information regarding the program of the annual meeting of the American Radium Society, address the President, Dr. Charles G. Stetson, 97 Lawrence Parkway, Tenafly, New Jersey.

The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine is owned maintained by, and in the interests of, the American Roentgen Ray Society, Inc. It is issued monthly by Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois. The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine does not hold itself responsible for any statements made or opinions expressed by any contributors in any article published in its columns.

Delivery is not guaranteed. Replacements are not guaranteed nor promised, but will be attempted if extra single copies are available and only if requested within 30 days from first of month following publication (17th of month) for domestic subscribers and 60 days for foreign subscribers.

Annual subscription price is as follows: United States, U. S. Possessions, U. S. Trusteeships, Pan-American Union, and Canada, $15.00; other countries $17.00. Prices for back volumes quoted on application. Extra single copies of back issues, if available, $1.50, postpaid. Current subscriptions may begin with any issue. Remittance should be sent to CHARLES C THOMAS, PUBLISHER, 301–327 East Lawrence Avenue, Springfield, Illinois, U.S.A.

ADDRESS CHANGE—When a change of address is necessary please allow at least 60 days notice and preferably 90 days. When ordering a change of address, send the Publisher both the old and new address.

Entered as Second-class at Springfield, Illinois under the
Act of March 3, 1879. Printed in U.S.A.

Second-class postage paid at Springfield, Illinois
and at additional mailing offices.

Copyright © 1963, by AMERICAN ROENTGEN RAY SOCIETY, Inc. No part may be duplicated or reproduced without permission of the Publisher.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 90 OCTOBER, 1963 NO. 4

CONTENTS

The Rates and Patterns of Growth of 375 Tumors of the Large Intestine and Rectum Observed Serially by Double Contrast Enema Study (Malmö Technique). SOLVE WELIN, M.D., JAMES YOUKER, M.D., AND JOHN S. SPRATT, JR., M.D., WITH THE PATHOLOGICAL CONSULTATION OF FOLKE LINNELL, M.D., HARLAN J. SPJUT, M.D., R. E. JOHNSON, M.D., AND L. V. ACKERMAN, M.D. 673

Schistosomiasis Mansoni: Roentgenologic Observations in a Nonendemic Area. ARNOLD CHAIT, M.D. 688

The Roentgen Findings in Strictures of the Colon Associated with Ulcerative and Granulomatous Colitis. RICHARD H. MARSHAK, M.D., CLAUDE BLOCH, M.D., AND BERNARD S. WOLF, M.D. 709

Demonstration of Fistulas by Vaginography. R. W. LAMBIE, M.D., S. RUBIN, M.D., AND D. S. DANN, M.D. 717

Vaginography. FRED O. COE, M.D. 721

Celiography with Iothalamic Acid; Experimental Studies in Dogs and Rats. ALEXANDER R. MARGULIS, M.D., GALEN B. COOK, M.D., GEORGE L. TUCKER, M.D., AND SIDNEY L. SALTZSTEIN, M.D. 723

The Roentgen Manifestations of Mesenteric Adenitis. M. H. POPPEL, M.D. 727

Intramural Hematoma of the Jejunum; A Case Report. GORDON J. CULVER, M.D., AND HERBERT S. PIRSON, M.D. 732

Pancreatic Cystadenoma with Intestinal Hemorrhage. H. ROSENBAUM, M.D., P. J. CONNOLLY, M.D., A. R. W. CLIMIE, M.D., AND W. S. REVENO, M.D. 735

Annular Pancreas in Infancy; Report of 3 Cases. NAIM K. ATALLAH, M.D., AND RAFIC E. MELHEM, M.D. 740

Dermatomyositis with Significant Involvement of the Gastrointestinal Tract. FRIEDA FELDMAN, M.D., AND RICHARD H. MARSHAK, M.D. . . 746

Adenoma of the Duodenal Bulb; A Case Report. CARL W. BOYER, JR., MAJOR, MC, USA, AND RICHARD B. HELFRICH, MAJOR, MC, USA 753

(Continued on p. iv)

Intraluminal Duodenal Diverticulum. J. C. H. Laudan, M.D., and G. I. Norton, M.D. 756
Acute Organo-Axial Gastric Volvulus. Leo S. Figiel, M.D., and Steven J. Figiel, M.D. 761
The "Ring" Shadow in the Diagnosis of Ulcer. Mortimer Lubert, M.D., and George R. Krause, M.D. 767
Gastroesophageal Retrograde Mucosal Prolapse; A Cause of Upper Gastrointestinal Hemorrhage. Charles J. Fagan, Captain, MC, US Army, and Eddy D. Palmer, Colonel, MC, US Army 774
Diagnostic Problems of Esophageal Cancer; Relationship to Achalasia and Hiatus Hernia. William B. Seaman, M.D., Josephine Wells, M.D., and Charles A. Flood, M.D. 778
Retrotracheal Lymphadenopathy in Bronchial Carcinoma, Revealed by the Barium-Filled Esophagus. Felix G. Fleischner, M.D., and Eckart Sachsse, M.D. 792
Esophageal Hiatus Hernia of the Stomach. John A. Martin, M.D. . . . 799
The Lower Esophageal Ring; Long Term Follow-Up of Symptomatic and Asymptomatic Rings. Richard Schatzki, M.D. 805
The Anatomic Basis for the Lower Esophageal Contraction Ring; Plication Theory and Its Applications. O. Arthur Stiennon, M.D. 811
Pharyngeal Cinefluorography in Clinical Practice. James H. Scatliff, M.D., and M. Peter Scibetta, M.D. 823
Internal Biliary Tract Fistulae. C. Jules Rominger, M.D., and Christopher W. Canino, M.D. 835
A Study of Fixed Filling Defects in the Well Opacified Gallbladder and Their Evolution. R. Vincent Grieco, M.D., Noel F. Bartone, M.D., and Anthony Vasilas, M.D. 844
Clinical Evaluation of a New Intravenous Cholangiographic Medium: 5,5'-Sebacoyl-diimino-bis (2,4,6-Triiodo-N-Methylisophthalamic Acid), A Preliminary Report. Thomas R. Marshall, M.D., and J. T. Ling, M.D. 854
Renal Insufficiency following Cholecystography. William B. Seaman, M.D., Stuart Cosgriff, M.D., and Josephine Wells, M.D. 859
Spatial Fluctuations of X-Ray Quanta and the Recording of Radiographic Mottle. K. Rossmann, Ph.D. 863
Officers 870

Editorials

Some Aspects of Television Radiology. George A. Kling, M.D. . . 871
Manuel F. Madrazo, M.D., 1890–1963. Guillermo Santín, M.D. . 874
Everett L. Pirkey, M.D., 1915–1963. J. T. Ling, M.D. 876
Peter E. Russo, M.D., 1904–1963. Bert E. Mulvey, M.D. . . . 878
News Items 880
Book Review 882
Books Received 882
Abstracts of Radiological Literature 884

the Windsor 90/15

runs circles around other X-ray tables:

for accessibility . . . for versatility . . . for fatigue-free fluoroscopy

. . . and nothing touches the new Windsor 90-15 for sophistication. Here, at last, is a hydraulic tilting mechanism for smooth, gliding stops . . . effortless touch control operation . . . a perfected island design that gives unprecedented freedom, allows unlimited, unobstructed patient examination.

And here in a simple, single-unit design, you have the one fluoroscopic tool that converts to a diagnostic aid for radiography and special procedures. A weight reducing overhead suspension . . . a completely removable spot film device and supporting tower — these make the Windsor 90-15 the one X-ray table to specify. The Windsor 90-15 was designed for radiologists by systems engineers . . . assuring the operator the freedom of function he needs, the professional perfection he wants.

Keleket's companion pieces to the Windsor 90-15 represent some of the most advanced concepts in quality X-ray apparatus. These system-engineered components function together with the Windsor 90-15 as a single working unit — made possible by Keleket's integrated manufacturing operation.

The X-ray Generators, the Image Intensifier Systems, and the Dynapoise Tube Crane — are just three of the full realm of equipment designed for precise dovetailing for optimum, comprehensive radiological facilities.

For product reliability, turn to Keleket: Coast to coast, the first name in X-ray since 1900 . . . complete with technical support assurance close at hand. For complete information, locate your local Keleket representative in the yellow pages, or write for the new Technical Data Sheet from Keleket/Tracerlab, your partners for progress in the life sciences.

See us at Booths 16-19, American Roentgen Ray Society Meeting

LFE

KELEKET

A DIVISION OF LABORATORY FOR ELECTRONICS INC.
WALTHAM 54, MASSACHUSETTS

- Medical X-ray Equipment
- Nuclear Instruments
- Film Badge Service
- Instrumentation Accessories & Supplies

CALCUTTA UNIVERSITY
CENTRAL LIBRARY

designed for the discriminating Roentgenologist

MITCHELL-HOFMANN
DIAGNOSTIC X-RAY EQUIPMENT

three phase generator

FEATURES . . .

Choice of Three Control Types:

1. Three-Controls — KV, MAS and MA.
   Manual Conventional
2. Two-Controls — KV and MAS.
   Semi-Automatic
3. One-Control — KV.
   Fully Automatic

EXCLUSIVE HOFMANN RADIOSET

- A moveable scale located between the KV and MAS scales permits easy setting and reading of range adjustments for normal, heavy or thin patients and is controlled automatically by the MAS product.
- Falling load compensation resulting in utilization of optimum tube loading during short exposure time in Lung, Stomach and other short time Radiography.
- Excellent performance of the generator — even on an unstable or weak line.

A Mitchell X-Ray Products Company representative will be glad to arrange for a demonstration of this generator in the Philadelphia area at your convenience.

MODEL SR-550

SPECIFICATIONS

Rating: 550 MA at 70 KV. 400 MA at 100 KV.
210 MA at 125 KV.
Tube Voltage: From 30 to 125 KV for Radiography.
From 35 to 90 KV for Fluoroscopy.
MAS Product: From 2 to 500 MAS Stepless Control by means of MAS relay.
Exposure Time: From 0.02 seconds to 8 seconds.
H.T. Outlets: For 2 tube operation.
Stabilization: Magnetic Voltage Stabilizer for Filament.
Electronic Stabilization for Line may be Furnished if Required.
Rectifier: Barrier-layer Selenium Rectifiers in Tandem 12 Valve Circuit.
Mains Connection: 380 Volts; 3 phase. 60 cy.
Mains Resistance: 0.5 Ohm.
DIMENSIONS: Control—35″ wide, 16″ deep, 35½″ high.
High Tension Transformer—
24″ wide, 12″ deep, 36½″ high.

MITCHELL X-RAY PRODUCTS COMPANY
354 EAST WASHINGTON STREET, NORRISTOWN, PENNSYLVANIA
Nondestructive Testing • Engineers and Consultants

Dealer Franchises
Available in
Some Areas.

For Information—
Write Box 857
Norristown, Pa.

the KEY

to reduced radiation exposure

Constant research, development and perfection in Gevaert laboratories today bring you as fine and fast a film as dedicated technicians can produce. Even with a sharp reduction in exposure, your Gevaert film will enlighten your view box with a radiograph of gratifying brilliance and clarity. Seeing is believing.

GEVAERT
X-RAY FILM

Exclusive Distributors:
LOW X-RAY CORPORATION
161 Sixth Avenue, New York 13, N. Y.

Other Offices:
Atlanta • Chicago • Houston • Los Angeles

NATIONWIDE WAREHOUSING

General Electric Teletrol... your "front window" on today's revolution in radiology

Who would imagine this radical new concept in diagnostic x-ray would gain acceptance so rapidly? General Electric TELETROL System—remote-control fluoroscopy and radiography—revolutionizes the radiologist's whole viewpoint—both figuratively and literally. Combines remote, radiation-free control of equipment and patient positioning, with all the most sought-after technical developments of recent years: electronic image intensification ... remote television viewing in consultations... and cinefilming as well as routine radiography with cassettes. Although no longer the only remote unit, G-E TELETROL continues to overshadow the others with inherent advantages that no comparable alternative approach can offer you.

THE AMERICAN JOURNAL
OF ROENTGENOLOGY
RADIUM THERAPY AND
NUCLEAR MEDICINE

Vol. 90 OCTOBER, 1963 No. 4

THE RATES AND PATTERNS OF GROWTH OF 375 TUMORS OF THE LARGE INTESTINE AND RECTUM OBSERVED SERIALLY BY DOUBLE CONTRAST ENEMA STUDY (MALMÖ TECHNIQUE)*

By SOLVE WELIN, M.D.,[1] JAMES YOUKER, M.D.,[2] *and* JOHN S. SPRATT, Jr., M.D.[3]
with the pathological consultation of
FOLKE LINNELL, M.D.,[4] HARLAN J. SPJUT, M.D.,[5] R. E. JOHNSON, M.D.,[6] *and* L. V. ACKERMAN, M.D.[7]

THE purposes of this paper are to report the rates of growth of different morphologic types of primary colonic and rectal neoplasms, to compare the rates of growth of the primary cancers with the rates of growth of pulmonary metastases from cancers of the colon and rectum and to use the observed rates of growth as a parameter for estimating the age of the neoplasms.

The feasibility of measuring change in size by serial mensuration of primary colonic tumors outlined by double contrast enema examinations has been reported previously.[17] The same technique has been applied to roentgenographically demonstrated shadows of pulmonary metastases from colonic and rectal carcinomas.[2] In both previous reports the assumption was made and in part confirmed that both the primary colonic tumors and the pulmonary metastases grew by a geometric progression in volume and that the time necessary for each doubling of the volume was a constant which Collins called the "doubling time." The doubling time of the only primary cancer observed by double contrast enema study was 636 days.[17] Recently, Figiel *et al.*[6] have reported roentgenographic observations on the slow growth of colonic cancers. The mean doubling time for 25 pulmonary metastases from primary cancers of the colon and rectum was 116 days.[2] These rates of growth characterize tumors of very long duration and a more detailed quantita-

---

* Supported by USPHS Grants No. C-5738 and CS-9741.

[1] Professor of Radiology, Roentgenodiagnostik Institute, Malmö Allmänna Sjukhuset, University of Lund, Sweden.

[2] Assistant Professor of Radiology, Medical College of Virginia, Richmond, Virginia.

[3] Chief Surgeon, Ellis Fischel State Cancer Hospital, Columbia, Missouri.

[4] Professor of Pathology, Malmö Allmänna Sjukhuset, Malmö, Sweden.

[5] Professor of Pathology, Baylor University School of Medicine, Houston, Texas.

[6] Chief Pathologist, Ellis Fischel State Cancer Hospital, Columbia, Missouri.

[7] Professor of Surgical Pathology, Washington University School of Medicine, St. Louis, Missouri.

TABLE I

TOTAL EXPERIENCE IN THE OBSERVATION OF TUMORS OF THE LARGE INTESTINE AND RECTUM BY DOUBLE CONTRAST ENEMA STUDY (MALMÖ MODIFICATION) (DECEMBER 1, 1953 TO JUNE 30, 1962)

No. of patients examined	16,177
Total no. of double contrast enema studies performed	21,043
No. of patients having tumors demonstrated	2,118
No. of patients having resections for tumors after first observation	479
No. of patients having presence of tumors verified at autopsy	53*
No. of tumors observed 2 or more times in 109 patients before resection of tumor	136†
No. of tumors observed 2 or more times in 194 patients, tumors still under observation	239‡
No. of patients having polypoid tumors observed roentgenographically without confirmation by resection, autopsy or second roentgen examination	1,283§

* Obligatory autopsy examinations are performed on all persons dying in the City of Malmö at the Pathological Institute of the Malmö Allmänna Sjukhuset.

† Total number patient days of observation = 113,430.
Minimal period of observation = 26 days.
Mean = 834 days.
Maximum period of observation = 3,859 days.

‡ Total number patient days of observation = 225,450.
Minimal period of observation = 65 days.
Mean = 939 days.
Maximum period of observation = 3,745 days.

§ Most not re-examined because tumors were smaller than 6 mm. in diameter.

tion of the rates of growth of different morphologic types growing primarily in the colon is very pertinent to a description of the natural history of such tumors.

MATERIAL

All material is from the Roentgendiagnostic Department and the Pathological Institute, Malmö Allmänna Sjukhuset, University of Lund, Malmö, Sweden, and from the Ellis Fischel State Cancer Hospital, Columbia, Missouri. The Malmö Roentgendiagnostic Department performs all of the roentgen diagnostic studies required on a stable population of 235,000 inhabitants of the city of Malmö. All persons included in this study were referred by physicians within the city or from other departments of the hospital. No systematic effort was made to perform cancer detection examinations on asymptomatic persons.

Between December 1, 1953 and June 30, 1962, all examinations of the large intestine and rectum were made with a double contrast enema technique (Table I). The preparation and examination involve the following steps: (1) light diet and 30 cc. of castor oil the day before the examination, (2) one plain water enema the evening before the examination, (3) atropine, 1 mg. orally, the morning of the examination followed 30 minutes later by a cleansing enema of plain water with clysodrast* added, (4) initial filling of the colon to the splenic flexure with thick barium containing clysodrast, (5) after each use of clysodrast, a toilet must be available since a complete colonic evacuation will occur within one minute, (6) after the last evacuation, the colon is filled only to the sigmoid flexure, (7) the colon is insufflated with air through a straight balloonless rectal tube until good distention is obtained, (8) the individual is rotated to ensure filling to the cecum, (9) residual barium in the rectum is evacuated with a tube, and (10) multiple roentgenograms are obtained including lateral decubitus, oblique, upright and anterior posterior projections. Fluoroscopy is employed only briefly to check the presence of barium throughout the colon. A standard tube film distance of 150 cm. is used for all projections, permitting comparison of changes in size on serial views and minimizing magnification.[20,21,22] The quality is dependent upon the thoroughness with which the colon is cleansed by clysodrast, the degree of colonic relaxation induced by the atropine, and the number of projections giving clear contrast for the entire colon including the cecum. Of the 21,043 examinations hitherto performed only 2 (0.009 per cent) have been complicated by perforation of the colon. Both perforations were below the peritoneal reflection and both healed spontaneously.[13]

---

* Ferrosan Malmö.

When the roentgenographic projection is made tangential to the intestinal wall from which the tumor is arising, intramural infiltration can be diagnosed. This infiltration results in indistinct or "infiltrative" margins for the roentgen shadow of the tumor and in time produces "indentation" of the intestinal wall (Fig. 1 and 2, *A–F*). When these roentgen diagnostic signs of infiltrating cancer were detected at the first examination, tumors have been resected in all but a few instances. Typical marginal infiltration and the correct diagnosis of cancer has been made for tumors as small as 3 mm. (Fig. 1). Among the 20 cancers shown in Figure 3, four had marginal infiltration diagnosed at the first examinations, 10 had marginal infiltration diagnosed during the period of observation, 5 cancers were never viewed by tangential roentgenographic projections of their bases and 1 polypoid carcinoma on a stalk did not develop the signs of infiltration. Thus, there exists a bias in the selection of tumors observed serially. Only the more polypoid shaped or protuberant tumors with distinct roentgen margins are available for serial observations (Fig 2 *B;* 4, *A*, *B* and *C;* and 5, *A–E*).

The greatest tumor diameter and examination dates of two or more double contrast enema studies have been recorded for the 136 tumors excised from 109 patients and the 239 tumors in 194 hitherto unoperated patients. The tumor outline was measured to the nearest millimeter on each margin. The total margin of error in determining diameter was therefore ± 2 mm. The error could vary from as much as 50 per cent for a 4 mm. tumor to as much as 3 per cent for a 60 mm. tumor. Only the same roentgenographic projection from each examination was used to ensure that serial measurements were comparable.

The time interval between examinations was recorded in days. The policy at Malmö has generally encouraged semiannual reexamination of patients harboring tumors, but this policy has not been followed strictly. The number of double contrast enema studies for each patient varied from 2 (215 patients) to 10 (1 patient). Only 10 tumors were observed for a total period of less than 6 months.

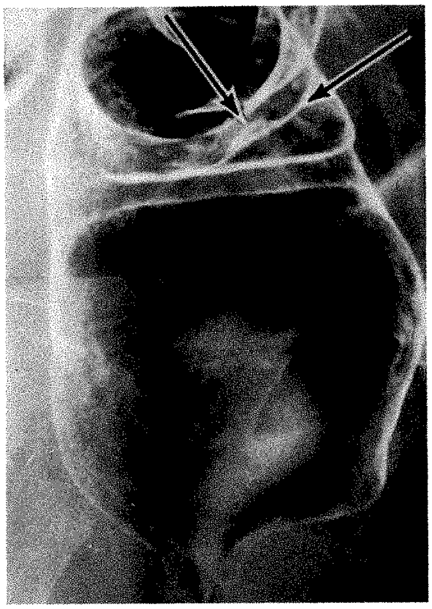


Fig. 1. An infiltrating primary carcinoma of the rectosigmoid 3 mm. in diameter was first diagnosed by double contrast enema study.

Similar mensuration was applied to 18 spherical pulmonary metastases observed in the serial thoracic roentgenograms of 11 patients having primary adenocarcinomas of the colon and rectum treated at the Ellis Fischel State Cancer Hospital. The doubling times of these metastases and 25 additional ones from Collins[2] are given in Table II.

Four pathologists reviewed the histologic sections of the excised tumors and classified the tumors independently according to their respective systems. Then, their classifications were matched to the rates of growth observed for the various tumors. The pathologists did not review the data on growth until they had committed their opinion on the tumor morphology.

INTERPRETATION

The collected data define changes in diameter over measured periods of time.

The mechanics of neoplastic growth are complex and we have measured the net results of new cell formation (the fundamental requisite for growth), cell death, cell dissemination away from the primary, and surface desquamation. Generally, unrestrained cellular proliferation proceeds by geometric progression, or exponential increase in the numbers of cells, the rate of increase being constantly proportional to the size already attained. When the number of cells, or synonymously the tumor size, approaches the limitations of nutrition, deceleration of exponential growth may occur. The former instance gives an upwardly concave growth curve and the latter a sigmoid growth curve (logistic or Gompertz curve) when plotted on arithmetic coordinates. The other variables acting simultaneously could alter the exponential growth to produce any of the variety of possibilities mentioned including arithmetic or linear growth in the diameter, random variation in growth, continued deceleration, continued acceleration or no growth.[1,4,5,9,14,18,19] The problem of determining the growth curves best-fitting the collected data becomes a complex statistical one.

First, the geometric configuration of

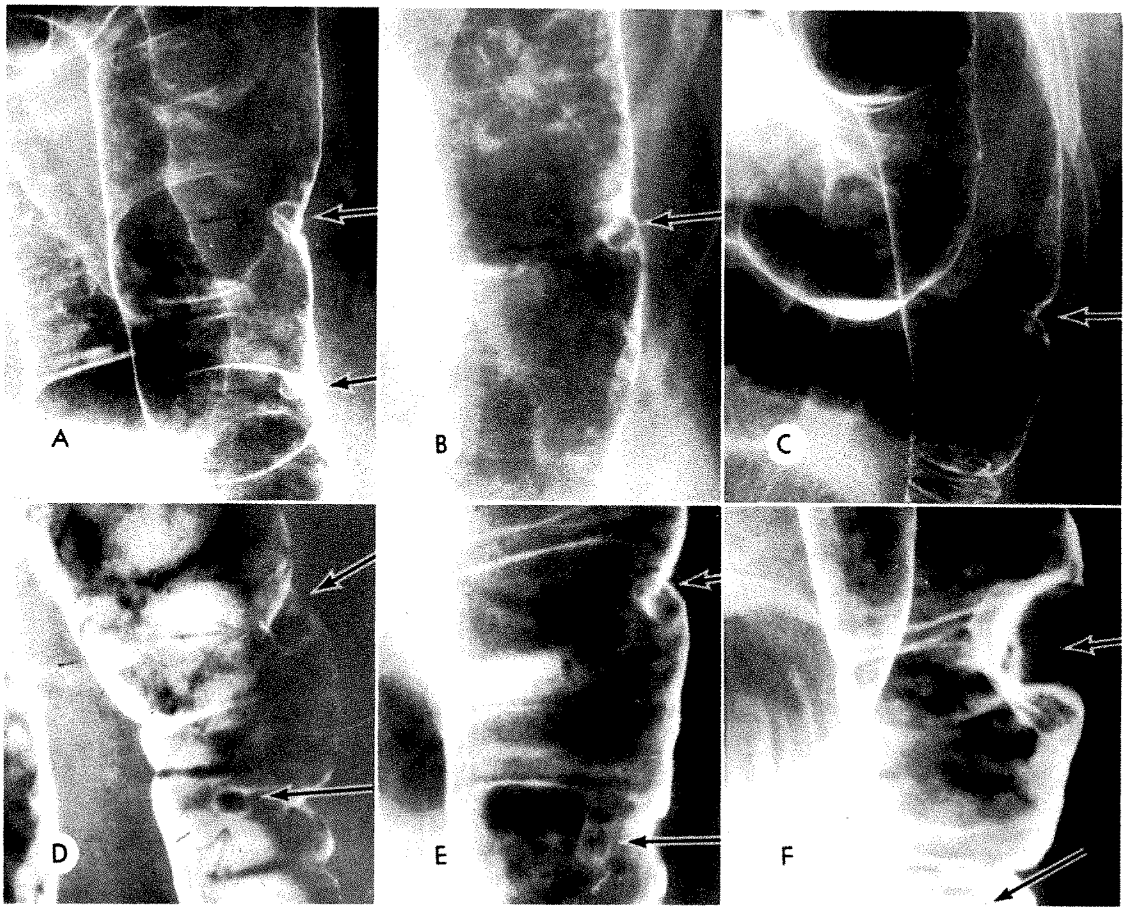


Fig. 2. Over 3.5 years of observation by double contrast enema studies, a polypoid tumor of 8 mm. grew into a 32 mm. symptomatic carcinoma in a 65 year old man (upper arrow). This tumor had from the first observation marginal infiltration and indentation of the tumor base, the roentgen diagnostic signs of cancer, when viewed tangentially. Simultaneously, a second polypoid tumor (lower arrow) showed neither growth nor infiltration during the period of observation. (*A*) November 18, 1953, (*B*) April 29, 1954, (*C*) December 13, 1954, (*D*) January 7, 1956, (*E*) March 7, 1956, (*F*) May 13, 1957.

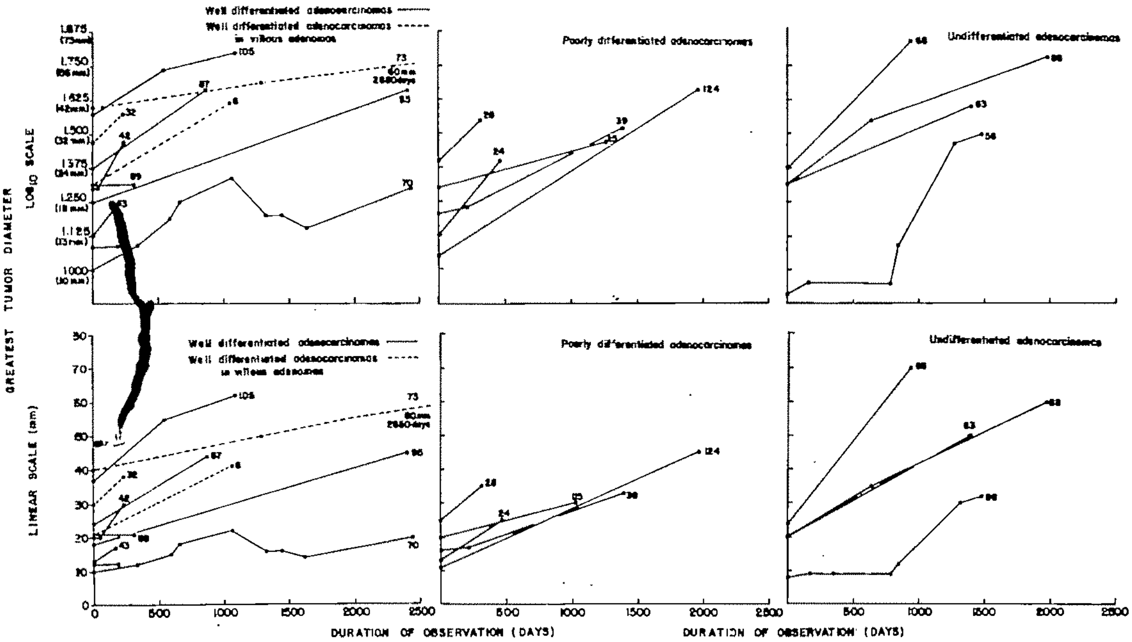


Fig. 3. Measured diameters plotted against time of observation with the diameters on a logarithmic scale (above) and on an arithmetic scale (below). With pure exponential growth the upper plots should form straight lines and with pure arithmetic growth of the diameter the lower plots should be linear.

growing colonic neoplasms must be known to relate the diametric measurements to changes in tumor volume. Most cancers of the colon and rectum grow over the mucosal surface of bowel as circumferentially spreading plaques (Fig. 6). The plaques may be ulcerated, sessile or pedunculated.[16] The plaques approach the geometric shape of cylinders ("medallion cancers") until they achieve a diameter of several centimeters. At this size some of them are prone to involve the entire circumference of the bowel ("napkin ring" cancers). These surface-spreading growths remain fairly constant in thickness and the changing volumes of the growing cancers are then proportional to the surface areas, the latter being proportional to the diameters squared. Consequently, for the purpose of this study we have regarded the diameters measured as being the diameters of the bases of cylinders of uniform thickness. More simply, we have regarded surface area as being proportional to volume for the purpose of calculating exponential growth constants and doubling times.

Figure 7 shows graphically the inability of these measurements to differentiate between linear and exponential diametric growth. An error of diametric measurement of only ±2 mm. would produce an overlap of exponential and linear growth curves

Table II

THE VOLUMETRIC DOUBLING TIMES OF PULMONARY METASTASES FROM COLONIC AND RECTAL ADENOCARCINOMAS

Doubling Time (days)	EFSCH*	No. of Metastases (Collins†)	Total
0–100	8	14	22
101–200	6	10	16
201–300	1	1	2
301–400			
401–500	1		1
Over 500	1		1
No growth	1		1
Total	18	25	43‡

* Eighteen pulmonary metastases from 11 patients seen at the Ellis Fischel State Cancer Hospital.

† Collins,[2] p. 390.

‡ Mean doubling time for the 43 metastases is 109 days.

during five-eights of the time necessary for a tumor to grow from a diameter of 3 mm. to a diameter of 60 mm. With a sigmoid shaped exponential growth curve (a Gompertz or a logistic curve), an overlap of the linear and exponential growth curves owing to random errors in measurement might exist throughout the roentgenographically visible existence of the neoplasms. Actually, no single tumor was observed long enough to exclude this overlap of growth curves from random errors in measurement of ±2 mm. The differentiation between linear and exponential diametric growth is indeterminable for the tumors observed only twice in 215 patients. Also, some tumors exhibited random variations in growth rate, further complicating a differentiation of growth patterns. The growth curves for the 20 cancers, plotted successively on linear and semilogarithmic graphs (Fig. 3) illustrate these points quite well. Consequently, we have considered that these cancers might have grown by either an exponential progression or a linear progression in tumor diameter and have calculated the mean rates of growth for both possibilities in their simplest mathematical forms.

The equation for growth by exponential or geometric progression in volume is

$$V_b = V_a e^{b(t_b - t_a)}, \qquad (1)$$

where V_a and V_b designate tumor volume at time t_a and t_b, e is the natural logarithmic base and b is the growth constant for the tumor.[5] This exponential equation may be approximated to growth data conforming to a Gompertz or a logistic growth curve above and below the points of inflection of these sigmoid curves.[19]

The exponential growth constant, b, is derived:

$$b_{ab} = \frac{\ln \dfrac{V_b}{V_a}}{t_b - t_a}, \qquad (2)$$

where ln is the natural logarithm. However,

$$\ln \frac{V_b}{V_a} \propto \ln \frac{d_b^2}{d_a^2} \quad \text{or} \quad 2 \ln \frac{d_b}{d_a}, \qquad (3)$$

where d is the diameter of the base of a cylindrical tumor of constant thickness.

Substituting (3) in (2) gives

$$b_{ab} = \frac{2 \ln \dfrac{d_b}{d_a}}{t_b - t_a}. \qquad (4)$$

The mean growth constant, b, for a series of observations of the same cancer is derived by taking the sum of the b's for each interval weighted by the number of days in

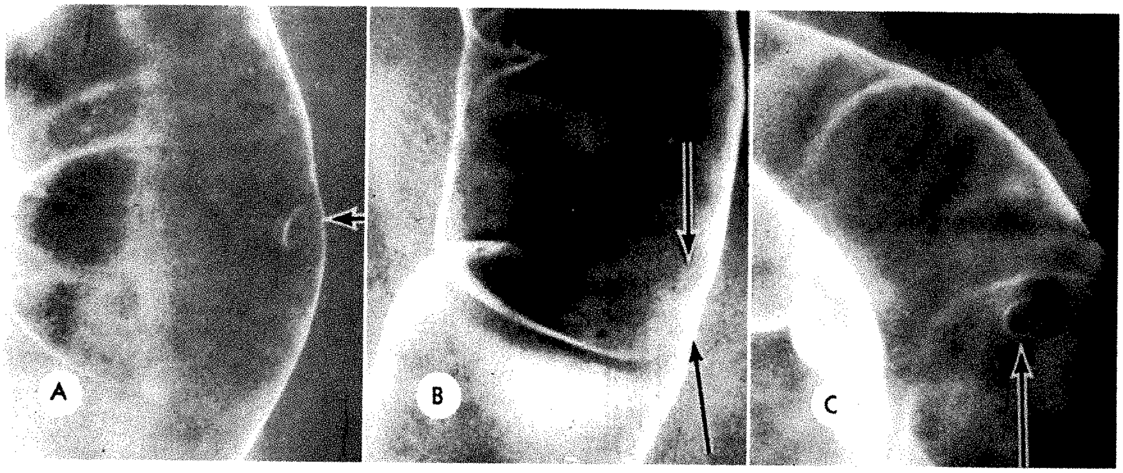


Fig. 4. A polyp of the descending colon 5 mm. in width in a 65 year old man showed no change in size or marginal configuration during 3 double contrast study observations over 6.5 years. (*A*) March 19, 1955, (*B*) June 23, 1960, (*C*) November 27, 1961.

the interval and dividing by the sum of the days in all intervals:

$$\bar{b} = \frac{b_{ab}(t_b - t_a) + b_{ac}(t_c - t_a) + b_{bc}(t_c - t_b)}{(t_b - t_a) + (t_c - t_a) + (t_c - t_b)}, \quad (5)$$

Substituting (4) in (5), we get

$$\bar{b} = \frac{2\left(\ln\frac{d_b}{d_a} + \ln\frac{d_c}{d_a} + \ln\frac{d_c}{d_b}\right)}{(t_b - t_a) + (t_c - t_a) + (t_c - t_b)}. \quad (6)$$

The procedure of weighting the growth rate of each interval by the duration of the interval in the determination of the mean growth rate is based on the probability that the rates of growth observed over longer periods of time are more likely to approach the true mean growth rate than are rates of growth observed over shorter periods of time. Errors in tumor measurement maximize the errors in growth rate determination when the period of time between tumor measurements is short.[1]

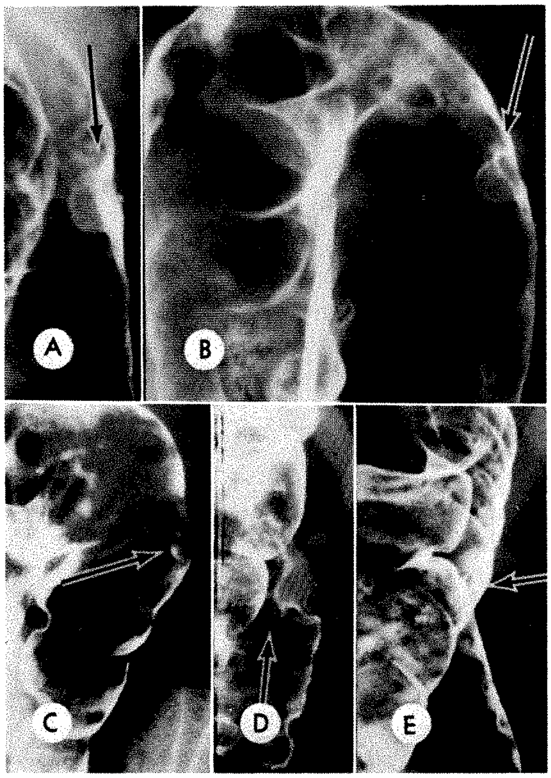


Fig. 5. Regression in size of a polyp in a five year old child from 9 mm. to 4 mm. during 4.5 years of observation. Similar though less striking regression has been observed in adults. (*A*) December 21, 1953, (*B*) August 8, 1955, (*C*) January 31, 1956, (*D*) August 16, 1957, (*E*) February 10, 1958.

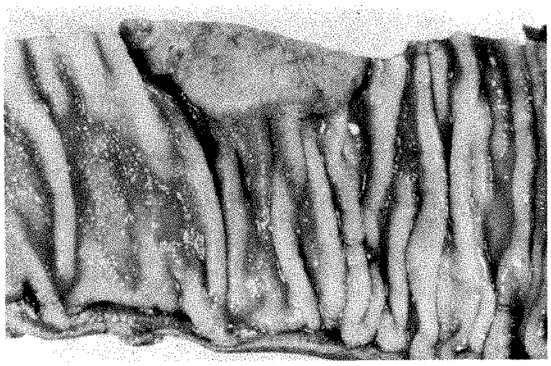


Fig. 6. Semicircle of a spreading plaque of cancer having uniform thickness. The cancer approximated the geometric shape of a cylinder maintaining uniform height while the diameter of its circular base enlarged in all directions.

The mean exponential diametric growth constant, $\bar{a}$, for cylindrical tumors reported in Figure 7 is derived

$$\bar{a} = \bar{b}/2. \quad (7)$$

Similarly, if growth of the diameter is by arithmetic progression, the mean linear rate of diametric growth, *R*, for a tumor observed *a*, *b*, and *c* times is calculated as follows:

$$R = \frac{(d_b - d_a) + (d_c - d_a) + (d_c - d_b)}{(t_b - t_a) + (t_c - t_a) + (t_c - t_b)}.$$

One-half of the linear diametric growth rate (Fig. 8) is the linear radial growth rate, *i.e.*, linear growth in mm./day from the central point of origin.

To derive the "doubling time", *D.T.*, the mean growth constant $\bar{b}$, is divided into the natural logarithm of 2:

$$D.T. = \frac{.69315}{\bar{b}}. \quad (8)$$

The doubling time is infinite for a nongrowing tumor and is negative for a regressing tumor. Interestingly, the reciprocal of $\bar{b}$ approximates the mean duration of the intermitotic life of a cell.[9]

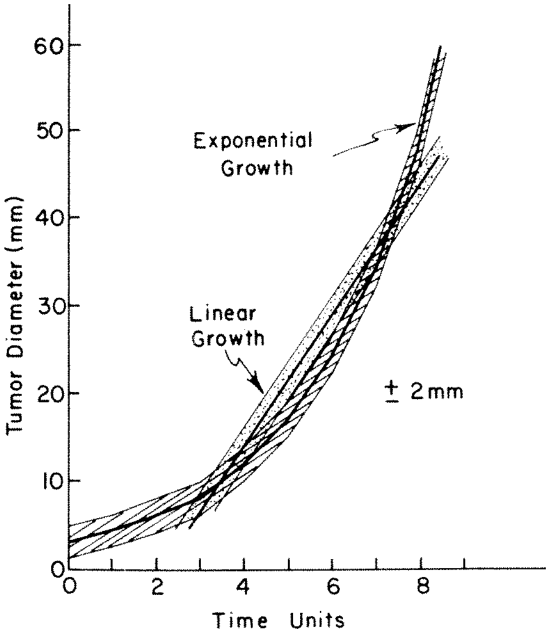


Fig. 7. Overlap of straight line and exponential diametric growth curves with an error in diametric measurement of 2 mm. during five-eighths of the time required for a tumor to grow from a diameter of 3 mm. to a diameter of 60 mm.

RESULTS

Only little difference occurred between the interpretations of the tumors by the different pathologists. The presence or absence of atypical changes in benign adenomatous polyps resulted in no change in the distribution of growth rates, and this morphologic alteration is probably of no consequence as far as rate of tumor growth is concerned. Spjut diagnosed a variant of polyp that he calls "villoglandular polyp." The villoglandular polyp contains a histologic mixture of adenomatous polyp and villous adenoma. These polyps were generally larger and their distribution of growth rates resembled that of villous adenomas. Consequently, they have been grouped with the pure villous adenomas. Not enough cancers were present in each category of differentiation to permit statistically significant conclusions regarding the influence of cancerous "differentiation" upon rate of growth.

The percentile frequencies of invasive cancers, villous adenomas and villoglandular polyps, adenomatous polyps and unresected tumors among the observed exponential and linear rates of growth are given in Figures 7 and 8. Figure 10 gives the percentage of invasive cancers among all tumors observed in each growth rate range. Obviously, a distinctive range exists that encompasses the mean rates of growth of 80 per cent of the invasive cancers and lesser percentages of the noninvasive tumors. On the linear scale this range extends from .003 to .025 mm./day and on the exponential scale from .0003 to .0025 for the exponential diametric growth constants. The latter is equivalent to a doubling time range from 1,155 to 138 days. These rates of growth are exceedingly slow; even the fastest growing cancer required 100 days to increase its diameter by only 2.5 mm. Consequently, double contrast enema studies should not be performed more often than

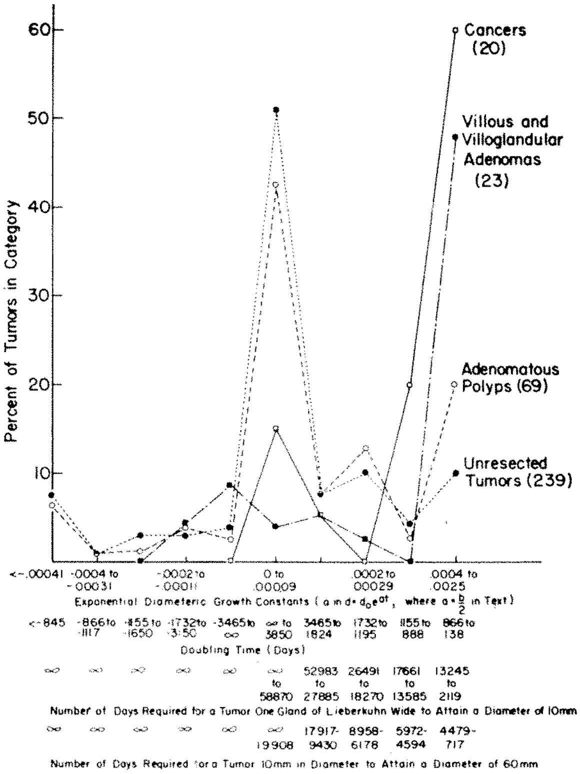


Fig. 8. Patterns of exponential diametric tumor growth.

every 100 days to detect an increase in size of the most rapidly growing polypoid cancer if our margin of error in measurement is ±2 mm. Growth was measurable in all cancers observed for at least 500 to 1,000 days though many noncancerous tumors observed for much longer demonstrated no growth.

The duration of these neoplasms must be known if we are to have any appreciation of their natural history. The time required for a tumor growing steadily at a known rate to increase a given amount in size is easily calculated. For tumors growing by an exponential increase in the diameter this interval is calculated,

$$t_b - t_a = \frac{\ln d_b - \ln d_a}{a},$$

and for a tumor growing by a linear increase in diameter

$$t_b - t_a = \frac{d_b - d_a}{R}.$$

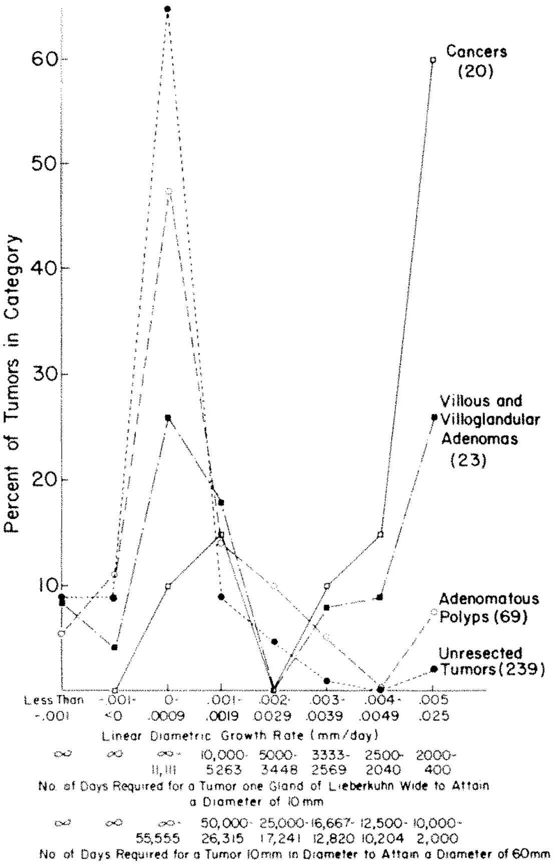


Fig. 9. Patterns of linear diametric tumor growth.

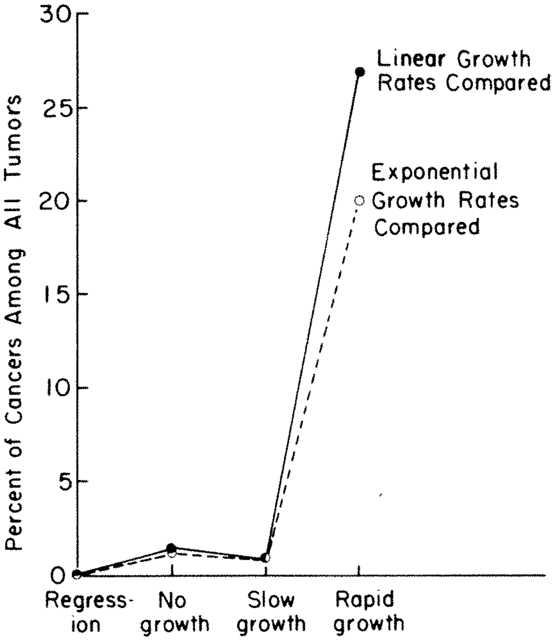


Fig. 10. Graphic quantitation of the percentage of cancers counted among all tumors in each growth rate range. Rapid growth of the tumor diameter is defined as (a) .003–.025 mm./day (linear scale), (b) .0003–.0025 exponential growth constant or 138 to 1,155 days volumetric doubling time (exponential scale).

The exponential diametric growth constant, *a*, and the linear rate of diametric growth, *R*, are known from Figures 8 and 9 respectively. Whether these rates of growth remain constant from the inception of the tumor is not known. Consequently, any estimation of the time required for a tumor to grow from the size of a single neoplastic gland of Lieberkühn to a 10 mm. diameter would be speculative. On the other hand any estimation of the time required for a tumor 10 mm. in diameter to grow to a size of 60 mm. in diameter would be based on more reliable data. The time required for a colonic or rectal neoplasm to grow over these two size intervals has been calculated for the corresponding rates of growth scales

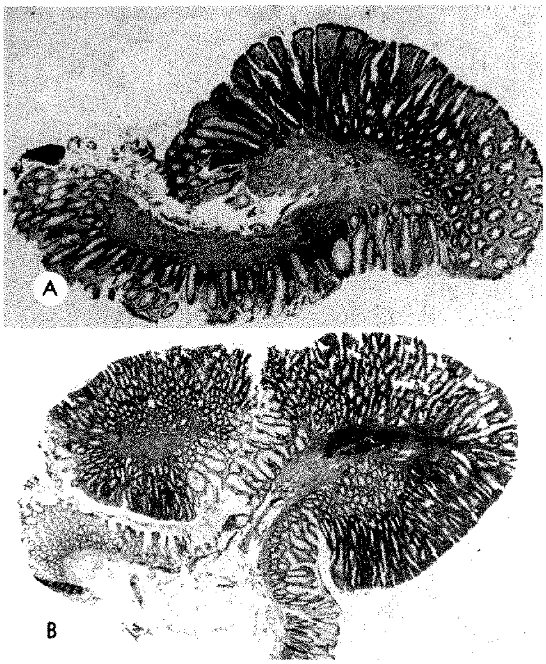


Fig. 11. (*A*) Morphologic appearance of a benign adenomatous polyp removed after 2,024 days of observation by double contrast enema studies. The polyp underwent no measurable growth during the 5.5 years of observation. (*B*) As measured on double contrast enema studies, this benign adenomatous polyp grew 1 mm. in diameter over 224 days of observation. This negligible growth could be attributable only to random error in measurement. All but one of the "rapidly growing" adenomatous polyps were of this type.

shown in Figures 8 and 9. Obviously, these tumors must have had very long periods of silent evolution before they become large enough to produce symptoms regularly. The fastest growing cancer thus far observed would have required 6 to 8 years to grow from glandular size to a diameter of 60 mm. The maximum human life span is about 40,000 days or 110 years and the slower growing cancers may have required well over half the maximum life time to attain the latter size.

The vast majority of the benign adenomatous polyps and the unresected tumors (most of which are probably benign adenomatous polyps) grew so slowly that they could not have achieved a significant size during the longest human life span (Fig. 8 and 9). These tumors were producing and desquamating new glandular cells without increasing in mass. To this extent they were behaving as normal intestinal epithelium. Sometime in the life history of these tumors they had to enlarge enough to become visible. Perhaps this occurred in the youth of the host when they could have increased their mass proportionately to the growth of the host. Indeed, adenomatous polyps are sometimes found in the children[7] and begin to appear with increasing frequency after the end of normal human growth.[8] These observations would favor the concept that adenomatous polyps are hamartomas, *i.e.*, of embyrologic origin being "primarily nonneoplastic, malformations or unborn errors of tissue development."[23] The complicated embryologic processes of intestinal lumenization with associated vacuolation, cyst formation, glandular coalescence, etc.[10] might reasonably be expected to leave vestigeal mucosal remnants or hamartomas. A basic genetic defect might present as Peutz-Jegher's syndrome or familial polyposis. In the absence of a basic genetic defect, adenomatous polyps or intestinal mucosal hamartomas might persist on a random chance basis distributed with greatest frequency in areas of the intestine exhibiting the greatest mucosal contortions in the embryo. These areas are the rectum and the vermiform process and cecum.[10] Per unit length the rectum and cecum are most prone to develop tumors in the adult.[18] The transformation of hamartomatous malformations to cancer occurs infrequently.[23] If these numerous small benign tumors of the human colon are not of congenital origin, the stimulus for their random development occurs during the youth of the host and the stimulus must occur almost ubiquitously among the populations of the United States and Europe.

A total of 17 adenomatous polyps had mean exponential rates of growth calculated to be in the same range as cancers. Twelve of these tumors were completely benign adenomatous polyps (Fig. 11, *A* and *B*) and 5 showed slight atypical change. Sixteen of the 17 tumors were observed under the conditions that maximize the errors in growth rate determinations; the tumors were of small size and were observed for relatively short periods of time. The seventeenth polyp was a large atypical adenomatous polyp that grew from a diameter of 34 mm. to a diameter of 42 mm. in 181 days the doubling time being 304 days. Neither invasion nor metastasis had occurred from this tumor, but if such growth were permitted to continue a bulky tumor would have developed. Only 8 of the adenomatous polyps, including the one just described, had linear diametric rates of growth of the same magnitude as cancers. Only 5 of these polyps were observed 3 or more times and none of them showed accelerating growth.

Forty-five per cent of the villous and villoglandular adenomas grew as fast as cancers and these tumors regularly became large. Because of their great size, extensive surface area involvement and cancerous rates of growth, villous adenomas have a greater statistical chance for becoming invasive and indeed the large villous tumors contain frequently areas of invasive cancers. Two of the 20 cancers in this study arose in villous adenomas. Neither of these villous adenomas containing invasive cancers underwent an acceleration in growth rate during the period of observation. In fact, only 1 cancer among all 20 observed underwent a seemingly abrupt acceleration of growth rate during the period of observation (Case 56, Fig. 3). However, the roentgen shadow showed typical marginal infiltration, the roentgen diagnostic sign of cancer, by the second of the seven double contrast enema studies when the cancer was only 9 mm. in diameter. In the specimen removed this was a highly invasive undifferentiated carcinoma with lymph node metastases (Fig. 12). No morphologic evidence of an antecedent benign tumor was found. The observation of the abrupt increase in growth rate depends on the accuracy of only two measurements of a tumor with an infiltrating indistinct margin and is therefore subject to question.

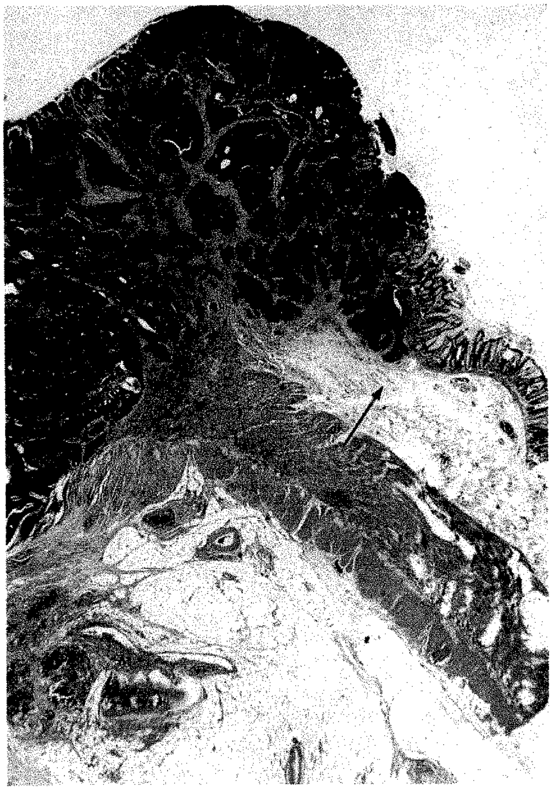


Fig. 12. This cancer (Case 56 in Fig. 3) grew from a diameter of 8 mm. to a diameter of 32 mm. over 1,474 days of observation by double contrast enema studies. The roentgen diagnosis of cancer was made when this tumor was 9 mm. in diameter because of the roentgen evidence of marginal infiltration. The tendency of a cancer to undermine normal mucosa adjacent the primary (arrow) is discernible by roentgenographic examination if the base of the cancer is viewed in a tangential projection during a double contrast enema study. Benign tumors as the adenomatous polyps in Figure 11, *A* and *B* do not undermine normal mucosa.

A gradation of growth rates corresponding to gradations of malignancy exists but an overlap of the spectrum of observed rates in each morphologic category occurs. Furthermore, a few tumors of no cancerous significance are found in each growth rate range (Table III). Consequently, rate of growth is not the only factor that determines whether a neoplasm of the large bowel or rectum will invade. True primary cancers invade while they are yet small tumors.[16] As mentioned, large sized, rapidly growing villous adenomas have a greater

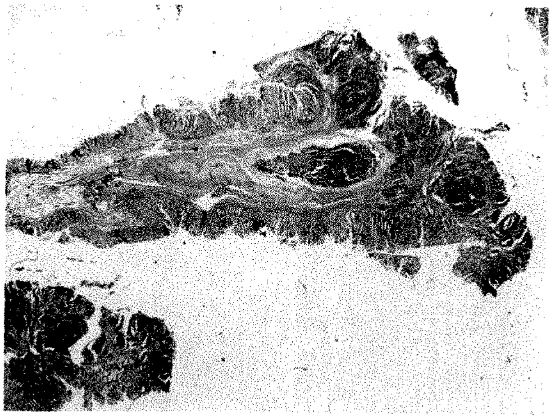


Fig. 13. This cancer on a well-formed pedicle fluctuated between 10 and 20 mm. in diameter as measured on 9 double contrast enema studies made at intervals over 7 years of observation. These measurements are shown in Figure 3, Case 70.

statistical chance of becoming invasive. The same might apply to the occasional, though relatively rare, rapidly growing adenomatous polyp. Other purely physical factors that might determine invasiveness and metastasization are the mechanical resistance of the host tissue, the rupturing pressure within the expanding neoplasm, and the mutual adhesiveness of the neoplastic cells.[3,11] The gross morphologic configuration of the tumor might affect and be affected by these physical factors. Greater cellular adhesiveness is associated with a more protuberant growth pattern.[3] Also, a polypoid tumor on a well formed pedicle, such as the polypoid cancer of Case 70 in Figures 3 and 13, has a greater ratio of surface area over volume than have more penetrating tumors. For 7 years this cancer was in an equilibrium state, varying between 10 and 20 mm. in diameter, and it invaded only through the muscularis mucosae and never metastasized. This pedunculated morphologic configuration would increase the likelihood of an equilibrium between the rate of cellular loss by desquamation and the rate of cellular gain from neoplastic cellular proliferation. The lateral expansile forces of a polypoid cancer would be expended into the lumen of the bowel rather than into the host. Conversely, a neoplasm with a more rapid rate of growth composed of less adhesive cells might begin in the depths of a crypt of Lieberkühn, rupture into the submucosa and begin reticular or infiltrative submucosal growth. Such a cancer might first present on the surface as an ulceration or might infiltrate extensively as linitis plastica.

Failure of slowly growing or static-sized noninvasive tumors to attain significant size during the human life span has practical significance in the diagnosis of colonic tumors demonstrated by double contrast enema studies. The measurement of fresh

Table III

RATES OF GROWTH OF INFLAMMATORY AND BENIGN NONEPITHELIAL NEOPLASMS OF THE RECTUM AND LARGE INTESTINE

	Rapid Growth*	Slow Growth	No Growth	Regression	Total
Amyloid tumor	1				1
Inflammatory polyp (granulation tissue)	2		2		4
Leiomyoma			1		1
Lipoma			1		1
Normal mucosa	3	1		1	5
Retention polyps	2	1			3
Specimen not available for second review†		2	5	2	9
Total	8	4	9	3	24

* .003–.025 mm./day diametric growth or an exponential doubling time of less than 1,155 days.
† All of these tumors were called "adenomatous polyps" on the original review.

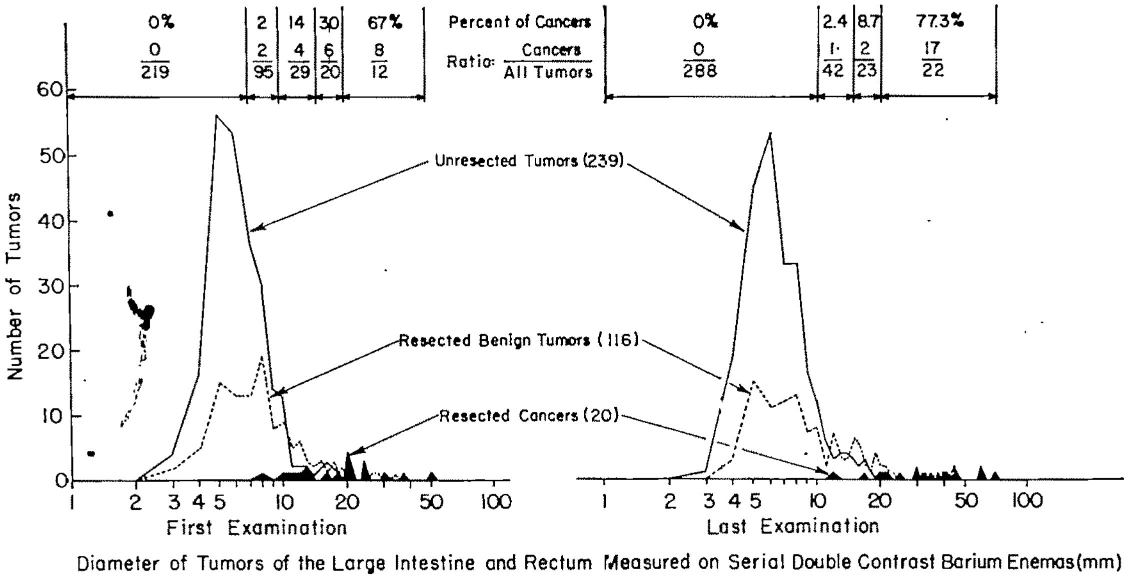


Fig. 14. The frequency distribution of the diameters of 375 colonic tumors measured on the first and last of a series of double contrast enema studies. The upper scale gives the frequency of known cancers observed in the bracketed size ranges. Resected benign tumors and cancers were observed for an average of 834 days and the unresected tumors for an average of 939 days.

tissue specimens of consecutively resected benign and malignant tumors showed that benign tumors exceed a diameter of 12 mm. infrequently.[15] With an error in roentgenographic measurement of ±2 mm., this critical dimension should lie in the vicinity of 10–14 mm. An analysis of the diameters of the 375 predominantly polypoid tumors in this study measured on the first and the last of the serial double contrast enema studies showed the critical roentgenographic diameter to be 10 mm. Tumors larger than 10 mm. were undergoing sustained growth and there was a great chance of their being invasive cancers (Fig. 14). One of the two cancers that was 10 mm. or less in diameter developed marginal infiltration before it attained a diameter of 10 mm., permitting the diagnosis of cancer. As previously observed the diagnosis of cancer has been made correctly on the basis of infiltrating margins in tumors as small as 3 mm. in diameter (Fig. 1). However, pedunculated cancers, cancers with well circumscribed or pushing margins and cancers arising in villous adenomas may not develop this sign until they are quite large and in these we must rely on size and growth to make the diagnosis of cancer. The statistical chance that any polypoid tumor attaining a roentgenographic diameter of greater than 10 mm. is cancer is so great that surgical resection is indicated on the basis of size alone. Search for other roentgen evidence of cancer would be superfluous. Tumors smaller than 10 mm. in diameter and appearing benign roentgenographically may be observed safely by serial double contrast enema studies. Only those that grow with a cancerous rate of growth or that exceed a diameter of 10 mm. on subsequent examinations will require resection. Among the numerous very small tumors (less than 8 mm. in diameter) that probably have no premalignant significance,[12,18] we may expect to find new cancers with the same low age specific incidence rates observed for the general population.[16] One exception is in children in whom single and multiple retention polyps regularly exceed a diameter of 10 mm. These have the roentgenographic signs of benign tumors and may be observed to the disappearance of the tumors.[20] All tumors accessible to sigmoidoscopic vision should have transendoscopic removal, no matter how small the tumor may be.

In the absence of data on the rates of growth of primary colonic and rectal cancers, the rather easily measurable rates of growth of pulmonary metastases from colonic and rectal cancers were known. Some speculation was entertained about the possibility that the primary cancers might grow at the same rate as the pulmonary metastases.[2,15] The doubling times of 43 spherical pulmonary metastases from carcinomas of the colon and rectum in 36 patients are shown in Table II. The median doubling time for the pulmonary metastases (Table II) is 109 days and for the 20 carcinomas is 620 days, a six-fold difference. The median linear radial growth is .02 mm./day for the pulmonary metastases and .004 mm./day for the primary cancers, the former rate being 5 times the latter. However, the pulmonary metastases shown in Table II and the primary cancers shown in Figure 3 did not occur in the same patients. Only 2 of the 20 primary cancers having doubling times of 323 and 550 days, respectively, have produced pulmonary metastases and in neither patient was the doubling time of the metastasis measured. Furthermore, those cancers of presumably greater malignancy and possibly more rapid growth that showed roentgen signs of infiltration while the cancers were still small are not available for serial observation. Whether the rate of growth of a cancer varies from organ to organ deserves further investigation since the answer is pertinent to understanding the dynamics of metastatic dissemination.

CONCLUSION

The rates of growth of 375 tumors of the colon and rectum have been calculated from the mensuration of the diameters of tumors observed serially by double contrast enema (Malmö) technique. There is a spectral overlap of growth rates for different morphologic types of tumors with cancers being distinctly predominant in the more rapid range. The cancerous rates are in the range of .003–.025 mm./day for linear diametric growth. If the growth is predominantly exponential, a point that cannot be resolved with certainty, the exponential diametric growth constant would vary from .0003–.0025 equivalent to a doubling time of 1,155–138 days. These very slow rates of growth would characterize tumors having many years of silent growth before attaining symptomatic size. Slower growing benign neoplasms of the colon and rectum might never attain significant size within the human life span. The mean rates of growth of the metastases in lung from colonic and rectal cancers are five to six fold faster than the mean rates of growth of the primary cancers growing in colon or rectum.

John S. Spratt, Jr., M.D.
The Ellis Fischel State Cancer Hospital
Columbia, Missouri

REFERENCES

1. Al-Doori, Y. Probability model for cancer growth. University of Missouri Computer Research Center, 1962 (unpublished) and personal communication.
2. Collins, V. P. Time of occurrence of pulmonary metastasis from carcinoma of colon and rectum. *Cancer*, 1962, *15*, 387–395.
3. Coman, D. R. Decreased mutual adhesiveness, a property of cells from squamous cell carcinomas. *Cancer Res.*, 1944, *4*, 625–629.
4. Davis, H. T. Problem of growth in two populations conflicting with one another. In: Introduction of Nonlinear Differential and Integral Equations. U. S. Government Printing Office, Washington D. C., 1960, Chap. 5.3, 99–102.
5. Defares, J. G., and Sneddon, I. N. Common growth and biology. In: An Introduction to the Mathematics of Medicine and Biology. The Yearbook Publishers, Inc., Chicago, 1960, Chap. VI, Sec. 5, 227–234.
6. Figiel, L. S., Figiel, S. J., and Wietersen, F. K. Is surgical removal of every colonic polyp necessary? Am. J. Roentgenol., Rad. Therapy, & Nuclear Med., 1962, *88*, 721–732.
7. Helwig, E. B. Adenomas of large intestine in children. *Am. J. Dis. Children*, 1946, *72*, 289–295.
8. Helwig, E. B. Evolution of adenomas of large intestine and their relation to carcinoma. *Surg., Gynec. & Obst.*, 1947, *84*, 36–47.
9. Hoffman, J. G. The Size and Growth of Tissue

Cells. Edited by O. Glasser. Charles C Thomas, Publisher, Springfield, Ill., 1953.

10. Johnson, F. P. Development of mucous membrane of large intestine and vermiform process in human embryo. *Am. J. Anat.*, 1913, *14*, 187–233.
11. Kellner, B. Progression of tumor growth and formation of metastases. *Acta morphol.*, 1961, *10*, 337–356.
12. Koppel, M., Bailar, J. C., III, Weakley, F. L., and Shimkin, M. B. Incidence of cancer in colon and rectum among polyp-free patients. *Dis. of Colon and Rectum*, 1962, *5*, 349–355.
13. Lorinc, P., and Brahme, F. Perforation of colon during examination by double contrast method. *Gastroenterology*, 1959, *37*, 770–773.
14. Mayneord, W. V. On a law of growth of Jensen's rat sarcoma. *Am. J. Cancer*, 1932, *16*, 841–846.
15. Spratt, J. S., Jr., and Ackerman, L. V. Relationship of size of colonic tumors to their cellular composition and biological behavior. *Surg. Forum*, 1960, *10*, 56–61.
16. Spratt, J. S., Jr., and Ackerman, L. V. Small primary adenocarcinomas of colon and rectum. *J. A. M. A.*, 1962, *179*, 337–346.
17. Spratt, J. S., Jr., and Ackerman, L. V. Growth of a colonic adenocarcinoma. *Am. Surgeon*, 1961, *27*, 23–28.
18. Spratt, J. S., Jr., Ackerman, L. V., and Moyer, C. A. Relationship of polyps of colon to colonic cancer. *Ann. Surg.*, 1958, *148*, 682–698.
19. Verhagen, A. M. W. Growth curves and their functional form. *Australian J. of Statistics*, 1960, *2*, 122–127.
20. Welin, S. Modern trends in diagnostic roentgenology of colon. The Mackenzie Davidson Memorial Lecture. *Brit. J. Radiol.*, 1958, *31*, 453–464.
21. Welin, S. Über die röntgenologische Untersuchung des Dickdarmes mit der Doppelkontrastmethode (Die Malmö Modifikation). *Radiologe*, 1962, *2*, 87–100.
22. Welin, S., and Lorinc, P. Das Röntgenbild des villosen (zottenformigen) Tumors in Bereich des Colons. *Radiologe*, 1962, *2*, 107–112.
23. Willis, R. A. Hamartomas involving endodermal epithelia. In: The Borderland of Embryology and Pathology. Butterworth and Co., Ltd., London, 1958, 372–373.

SCHISTOSOMIASIS MANSONI: ROENTGENOLOGIC OBSERVATIONS IN A NONENDEMIC AREA*

By ARNOLD CHAIT, M.D.
BROOKLYN, NEW YORK

THE epidemiologic, clinical, pathologic and roentgenologic manifestations of schistosomiasis have been extensively reported from many parts of the world. Until recently, however, this disease has been of only academic interest on this country's mainland. Large movements of population have introduced those of us in practice in large eastern urban centers to frequent contact with patients in various stages of infestation. It has been estimated on the basis of stool examinations that the incidence of schistosomiasis in school children in Puerto Rico averages about 10 per cent.[46] That this figure may be somewhat low is suggested by another report of 27 positive cases out of 52 consecutive unselected autopsies.[27] However, using the lower figure, it seems likely that at least 75,000 of the approximately 750,000 Puerto Rican immigrants to New York City are infected.[41] Mixed infections with *Necator americanus*, *Ankylostoma duodenale*, *Ascaris lumbricoides*, *Trichuris trichiura*, *Endamoeba histolytica*, *Endamoeba coli* and *Endolimax nana* are common.[23,46]

MATERIAL

Kings County Hospital Center is a New York City Municipal Hospital with a large and increasing Puerto Rican population. Although it has not been our practice routinely to investigate all Puerto Rican patients for schistosomiasis, in the 10 year period from 1952 to 1962 such a diagnosis has been established in 92 patients, either by rectal biopsy, stool examination, liver biopsy, at laparotomy, thoracotomy or autopsy. This does not include diagnoses made in several instances on compelling clinical grounds without histologic confirmation. Ninety of the 92 patients were of Puerto Rican origin and their parasite was demonstrated to be, or was assumed to be, of the *S. mansoni* species. One patient was Filipino and was infected with *S. japonicum*. One patient was Chinese, and was infected with *S. mansoni*. None of our cases were from areas endemic for *S. haematobium* and, as might have been expected, in none did we demonstrate bladder papillomata or bladder or ureteral calcifications.[30,36] Most of the infected patients had symptoms explainable on the basis of schistosomiasis. The number of undiagnosed infested patients whom we have treated for unrelated diseases or with unrecognized manifestations of schistosomiasis is conjectural.

EPIDEMIOLOGY, LIFE CYCLE AND PATHOGENESIS

The lesions of schistosomiasis may be so widespread and in such seemingly unrelated locations that a knowledge of the life history of the causative agent is essential for a thorough understanding of the disease. The three major trematodes responsible are *S. mansoni*, *S. japonicum* and *S. haematobium*. Their life cycles are similar, but we will confine our remarks to the first. *S. mansoni* is geographically widely distributed from Africa and Arabia to the West Indies and the northern part of South America.[19,30] Man is the definitive host of this blood fluke and is infected by the fresh water, free swimming cercarial form which is capable of penetrating the intact skin or buccal mucosa, but is destroyed by gastric secretions. This invasive stage may produce pain at each site of entry and urticaria.[19,45] Once gaining entrance to the body, the larvae, now known as metacercariae, reach the right side of the heart directly via the systemic venous circulation or via the lymphatics. They are small enough to pass through the lung capillaries without causing any permanent local damage, but, cough, angioneurotic edema, headache, nausea, malaise and neck stiffness have been reported and are presumed due to this transit. There may also be "mottling" on chest roentgenograms.[5] It must be emphasized that this early lung passage is not responsible for the granulomatous lung changes or vasculitis to be described later, and because of its occurrence shortly following infection, is rarely seen in nonendemic regions.

---

* From the Departments of Radiology of the State University of New York, Downstate Medical Center, and the Kings County Hospital Center, Brooklyn, New York.

After arriving in the systemic circulation, the larvae are widely disseminated, but, it has been assumed, only those which are distributed to the drainage area of the portal venous system will reach maturity.[18] In the intrahepatic portal veins they develop into mature male and female worms. This period may be characterized by generalized abdominal discomfort, late afternoon temperature elevation, night sweats and diarrhea.[19] The adult worms may be maintained in the portal system for 20 to 30 years or more,[41,46] thus explaining the fact that the disease may be active in a patient many years removed from the country of infection. They migrate against the portal blood flow into peripheral branches of the portal system, in the case of *S. mansoni*, usually into branches of the inferior mesenteric vein. The female deposits her ova in the smallest colonic or rectal venules.[19,34] Those ova which lodge in the colonic wall cause a granulomatous reaction. Those which reach the lumen are extruded with the stool, and hatch in fresh water freeing the miracidia. Each miracidium, following passage through a suitable snail intermediate host and metamorphosis into first and second generation sporocysts, develops into thousands of cercariae, the infectious form, thereby completing the cycle.[26,30]

Many of the ova are unsuccessfully deposited in the colonic wall and are washed back with the portal flow into the liver, where a periportal granulomatous reaction, similar to that in the colon, occurs. This is characterized by giant cells, epithelioid cells, lymphocytes, plasma cells and large numbers of eosinophils.[25,26] The eventual sequel is one of so-called pipestem cirrhosis[3,25] with splenomegaly and the formation of portal-systemic collaterals, such as esophageal varices. Via these collaterals, or via portal-systemic collaterals in the hemorrhoidal venous plexus, ova may reach the pulmonary arteries. The resultant pulmonary arteriolitis and arteriolar compression by granulomata may eventually result in pulmonary hypertension and cor pulmonale. Ova within the pulmonary parenchyma occasionally cause diffuse granulomatosis of the lung.[26,41]

Thus the major lesions of the disease, granulomatous reaction of the colon and rectum, cirrhosis with splenomegaly, portal hypertension with esophageal varices, pulmonary granulomatosis and pulmonary arteriolitis with pulmonary hypertension and right heart failure, are readily explained. It is more difficult to account for the so-called "ectopic" lesions, those found at sites apparently unrelated to the parasite's usual habitats, and often bearing no relationship to the portal venous system. Granulomatous lesions, and indeed adult worms, have been found in many bizarre locations including the thyroid, pancreas, myocardium, kidneys, ovaries, fallopian tubes, testes, cervix uteri and adrenals.[2,25] Lesions in the esophagus, stomach and duodenum, while generally classified as ectopic, admit of ready explanation on the basis of what has already been stated. The spleen, although of apparently easy access to a parasite of the portal system, is unaccountably but rarely the site of ovum or adult worm deposition, although such lesions have been described.[2] The splenomegaly so often seen is the result of chronic passive congestion and is not due to primary splenic involvement.

Middlemiss[30] assumes that the larvae are capable of maturing outside the portal bed, thus explaining the ectopic sites. The presence of a patent foramen ovale would also account for the systemic distribution of eggs and consequently of granulomata. Passage of ova through the vertebral venous plexus will also explain some of the ectopic lesions.[18] A perhaps more satisfying explanation has been offered by de Faria[16] and by de Faria *et al.*[17] who demonstrated pulmonary arteriovenous fistulae caused by schistosome ova which embolized in small pulmonary arteries causing necrosis of their walls and the walls of adjacent pulmonary veins.

I. RECTUM, COLON AND APPENDIX

ILLUSTRATIVE CASES

CASE I. J.F., a lethargic, weak 25 year old Puerto Rican male (K.C.H. No. 86299), was admitted on January 20, 1960, complaining of rectal bleeding, mucoid diarrhea and crampy abdominal pains of 5 months' duration. He had been in New York for 2½ years. His hemoglobin was 10.5 gm./100 ml., with an 18 per cent eosinophilia. Sigmoidoscopy revealed a polyp at 15 cm. which was biopsied and found to contain schistosome ova (Fig. 1). No other mucosal abnormalities were seen. On barium enema examination, a constant narrowing was visualized at the approximate rectosigmoid junction (Fig. 2), and the sigmoid colon appeared shortened and rigid (Fig. 3). No polyps were demonstrated.

CASE II. L.G., a 19 year old Puerto Rican male (K.C.H. No. 117968), was admitted for the first time on September 14, 1960, complaining of mucoid diarrhea and a 20 pound weight loss in 6 months. He had been in the United States for 1 year. Proctologic examination demonstrated hemorrhagic granulation tissue at the inferior valve of Houston. Schistosome ova

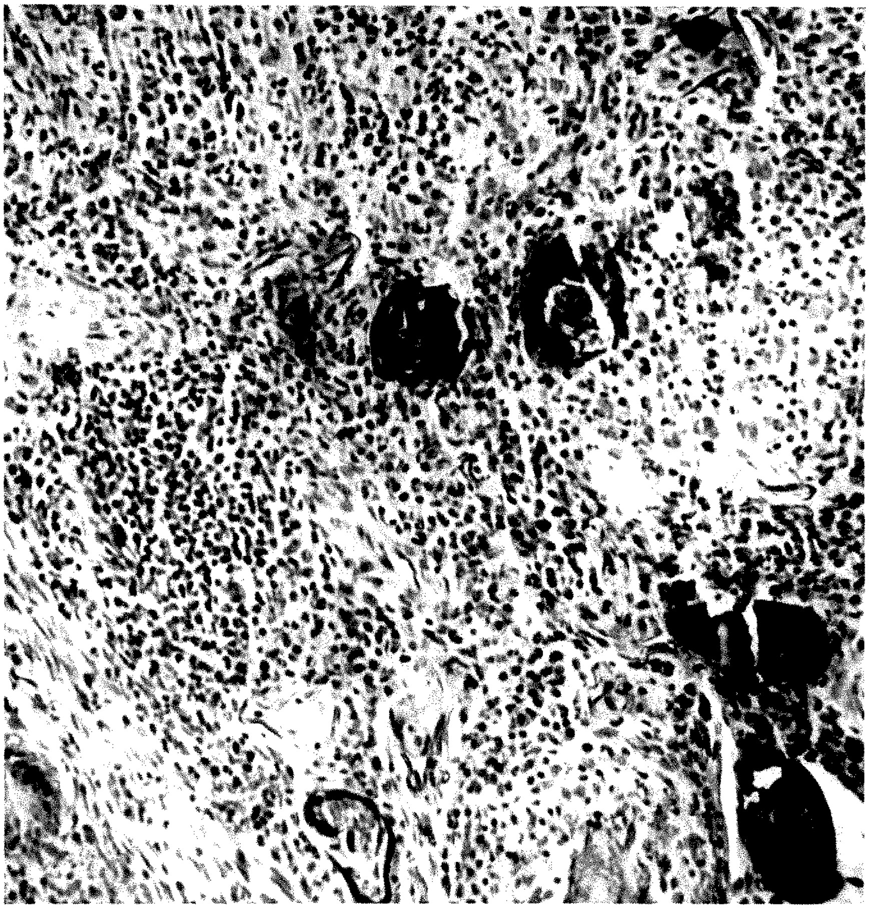


FIG. 1. Case I. Photomicrograph of section of rectum; calcified ova in the submucosa. Eosinophilic infiltration is prominent (hematoxylin and eosin, × 110).

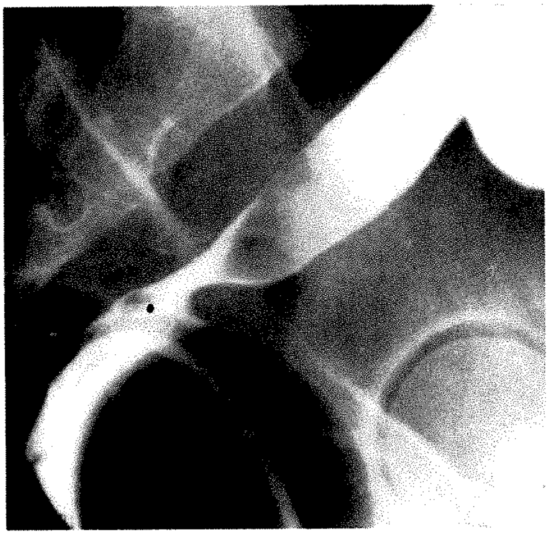


Fig. 2. Case i. Rectal constriction, constant on all barium enema roentgenograms.

and those of *N. americanus* were found in the stool. Rectal biopsy yielded chronic inflammatory tissue containing schistosome ova. Barium enema studies showed a peculiar granularity of the mucosa throughout the colon, apparently due to numerous punctate mucosal ulcerations (Fig. 4 and 5). The patient was re-admitted several months following his initial discharge with an acute perforation of the appendix. The surgical specimen was reported as evidencing acute ulcerophlegmonous appendicitis. A final

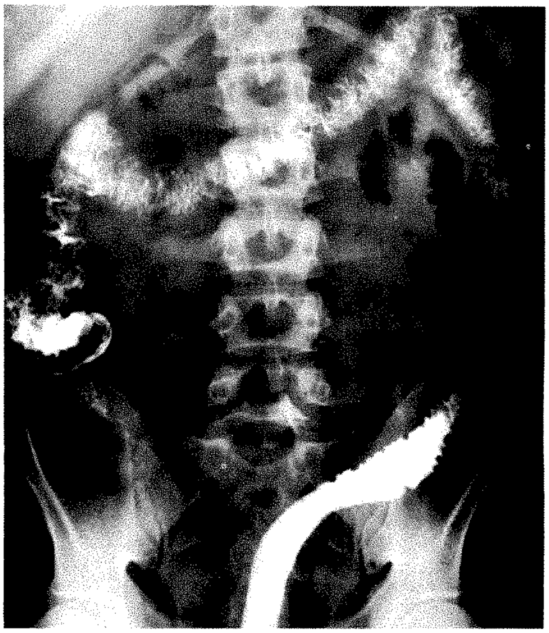


Fig. 3. Case i. Rigidity and shortening of the sigmoid colon.

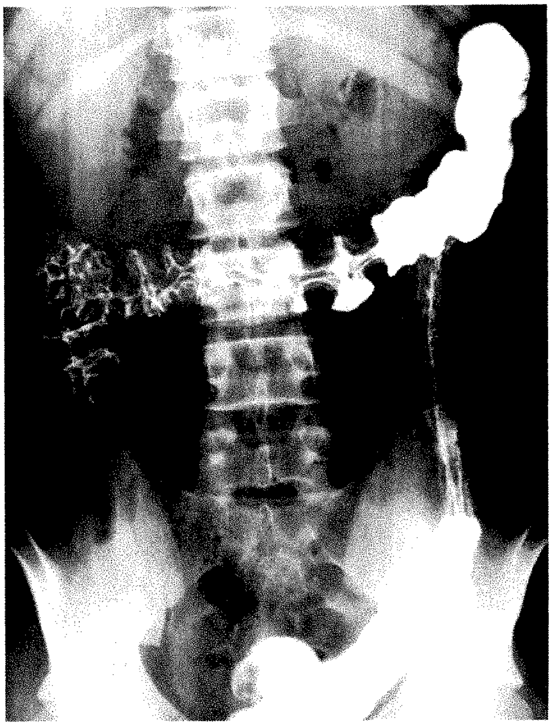


Fig. 4. Case ii. The mucosa of the descending colon has been thrown into longitudinal folds and minute punctate collections of barium, representing small areas of ulceration, are present throughout the colon.

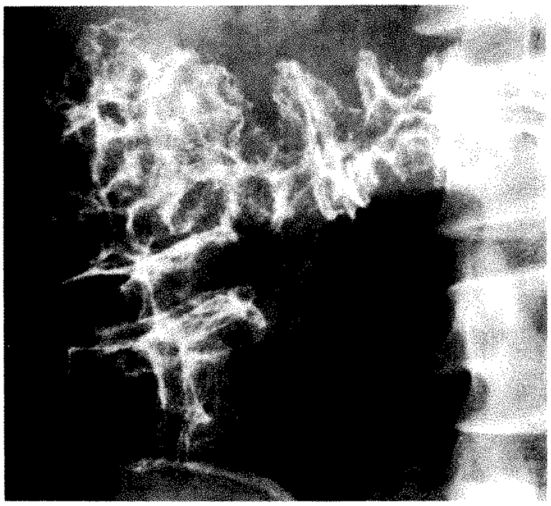


Fig. 5. Case ii. Detail of the right hemicolon; mucosal ulceration is demonstrated to better advantage.

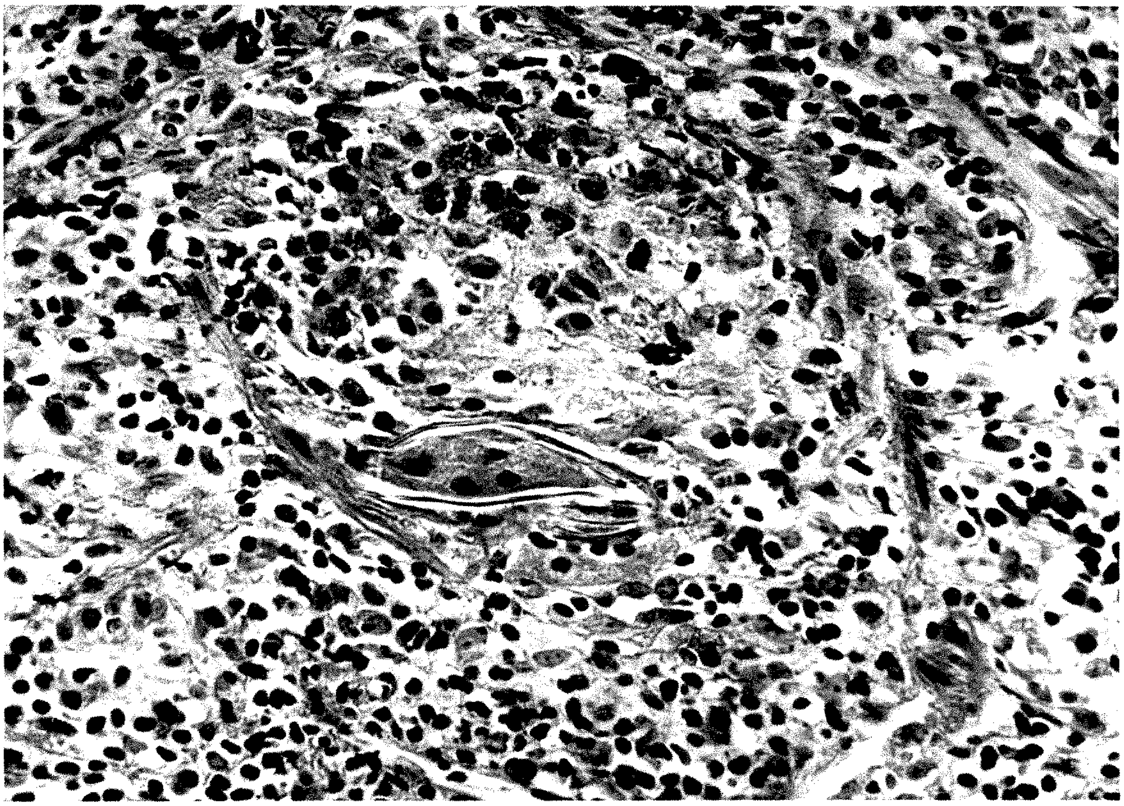


Fig. 6. Case iii. Photomicrograph of rectal submucosa: schistosome ovum surrounded by eosinophil-rich infiltrate (hematoxylin and eosin, ×260).

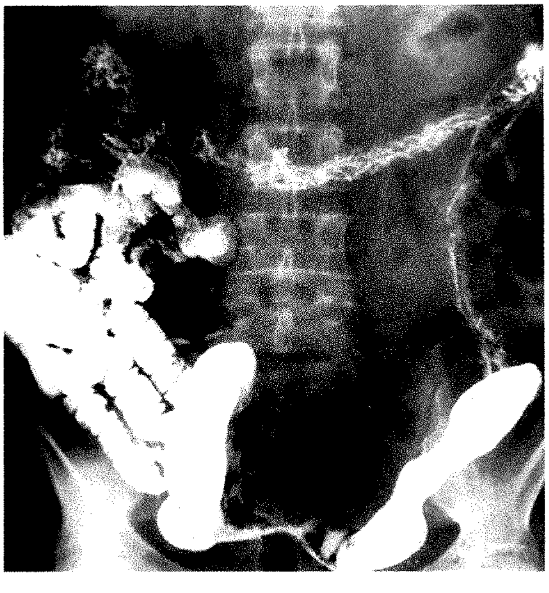


Fig. 7. Case iii. Rectosigmoid stricture demonstrated on barium enema study, confirming similar finding on proctoscopy.

admission was required because of schizophrenic tendencies and an obsessional character disorder.

Case iii. A.N., a 64 year old Puerto Rican female (K.C.H. No. 30414), was admitted on August 22, 1958, because of right upper quadrant pain radiating to the back, and fatty food intolerance for a period of 2 years. She had had two episodes of rectal bleeding 6 months prior to admission. Proctoscopy revealed a stricture at 5 inches, and the initial clinical impression was one of a malignant constriction of the rectum. The rectal mucosa was congested and edematous and rectal biopsy was positive for schistosome ova and granulomata (Fig. 6). Barium enema study confirmed the presence of a stricture at the junction of rectum and sigmoid (Fig. 7).

Case iv. R.M., a 42 year old Puerto Rican male (K.C.H. No. 12293), was admitted on March 16, 1962, because of right lower quadrant pain and diarrhea for a period of 2 days; on close questioning, he admitted to a 19 year history of episodic abdominal pain and vomiting. On physical examination there was moderate guarding in the right lower quadrant and slight rebound tenderness. The bowel sounds were hypoactive. Barium enema examination showed mucosal irregularity of the cecum and ascending colon with mural spiculations and considerable spasticity. The remainder of the colon appeared normal (Fig. 8 and 9). Eosinophils made up but 2 per cent of the total white blood cell count. A clinical diagnosis of acute appendicitis was made, and at laparotomy the cecum was found to be encased in a "fibrous wall" approximately 0.5 cm. thick, ascending the colon for approximately 4 inches and involving the periappendiceal tissues. The surgical specimen revealed schistosome ova and granulomata in the appendix and meso-appendix (Fig. 10) and the presence of an entirely serosal intensely eosinophilic granulomatous exudate in the pericecal fat, suggesting the recent demise of an adult female worm outside the wall of the cecum. Subsequent rectal biopsy was positive for schistosome ova.

CASE V. J. R., a 45 year old Puerto Rican female (K.C.H. No. 132485), was admitted on May 28, 1961 because of abdominal pain, vomiting and diarrhea. She had been in the United States since 1949. Her pertinent past history included a hospital admission elsewhere in 1959 for anemia (hemoglobin 4 gm. per cent), malaise, and a 20 pound weight loss. Her liver and spleen were both felt to be enlarged at that time. Bleeding from esophageal varices was diagnosed and a splenorenal shunt was attempted. This was unsuccessful because of laceration of the renal vein. A 460 gm. spleen was removed. Portal pressure was recorded as 250 mm. of saline. On admission to Kings County Hospital, the finding of esophageal varices was confirmed and schistosome ova were found on rectal biopsy. Eosinophilia was 23 per cent. Barium enema studies showed edematous mucosa and some rigidity and incomplete distention of the transverse colon on introduction of air (Fig. 11 and 12). An anastomosis of the end of the portal vein to the side of the inferior vena cava resulted in a reduction of the portal pressure from 360 to 180 mm. of saline 15 minutes after the performance of the shunt (normal: 150 to 200 mm. of saline). A liver biopsy was reported as showing postnecrotic cirrhosis.

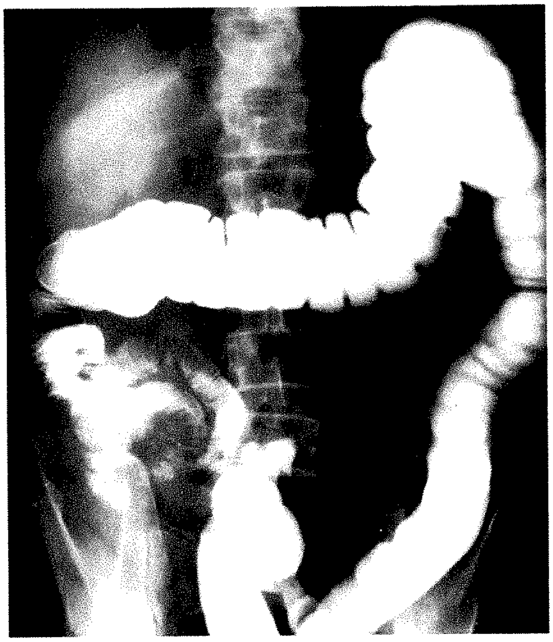


FIG. 8. Case IV. Mucosal irregularity of the cecum and ascending colon with mural spiculations and spasticity. Extensive pericolonic fibrosis was found at surgery.

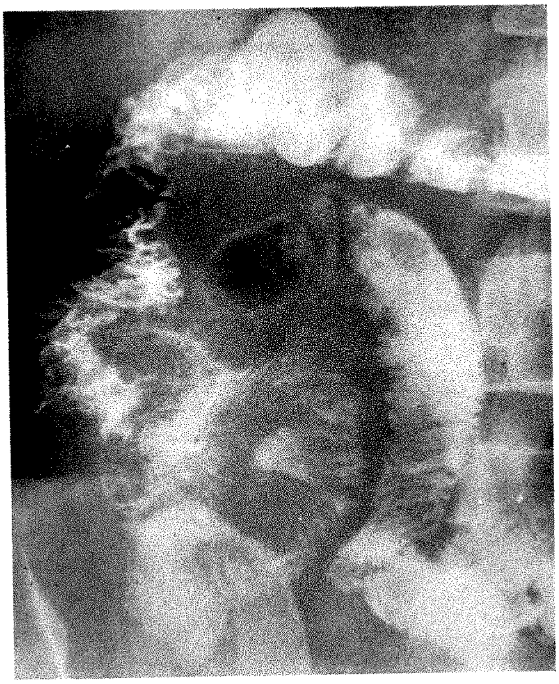


FIG. 9. Case IV. Detail of right hemicolon on partial evacuation of barium.

27/585

Case vi. P.D., a 37 year old Puerto Rican female (K.C.H. No. 5548), was admitted on 8 occasions between 1957 and 1961 with varying degrees of abdominal pain, of which she had been complaining for 12 years. She had lost 20 pounds during this period. Her appetite was good and bowel movements were normal. There had been 5 or 6 hospital admissions elsewhere in New York City and she had been operated upon previously in Puerto Rico. No cause for the abdominal pain had been reported. There had been one episode of hematemesis in the past. During the patient's first admission in 1957, a rectal biopsy revealed the presence of schistosome ova. A splenoportogram was normal. Barium enema studies at this time showed marked mucosal irregularity, edema and spasticity (Fig. 13 and 14). Between 1959 and 1961 there was roentgen evidence of progressive splenomegaly (Fig. 15 and 16). Despite multiple admissions, therapy was not successful in relieving her symptoms, the patient leaving the hospital frequently against advice. She was last seen in November, 1961, with a persistent hypochromic anemia.

DISCUSSION

The results of schistosomiasis of the colon and rectum depend upon the degree and duration of infestation. Types of involvement vary from occult forms with no bowel symptoms to clinically manifest forms categorized by Recio[37] with the descriptive terms of catarrhal, suppurative, ulcerative, adenomatous and granulomatous coloproctitis. This classification is based upon *S. japonicum* infection but should be valid for *S. mansoni* as well. A report from Yemen[11] states that 42 per cent of roentgen examinations show a "mucous colitis" due to *S. mansoni*. This diagnosis was based upon findings of spasm, edema, loss of haustra-

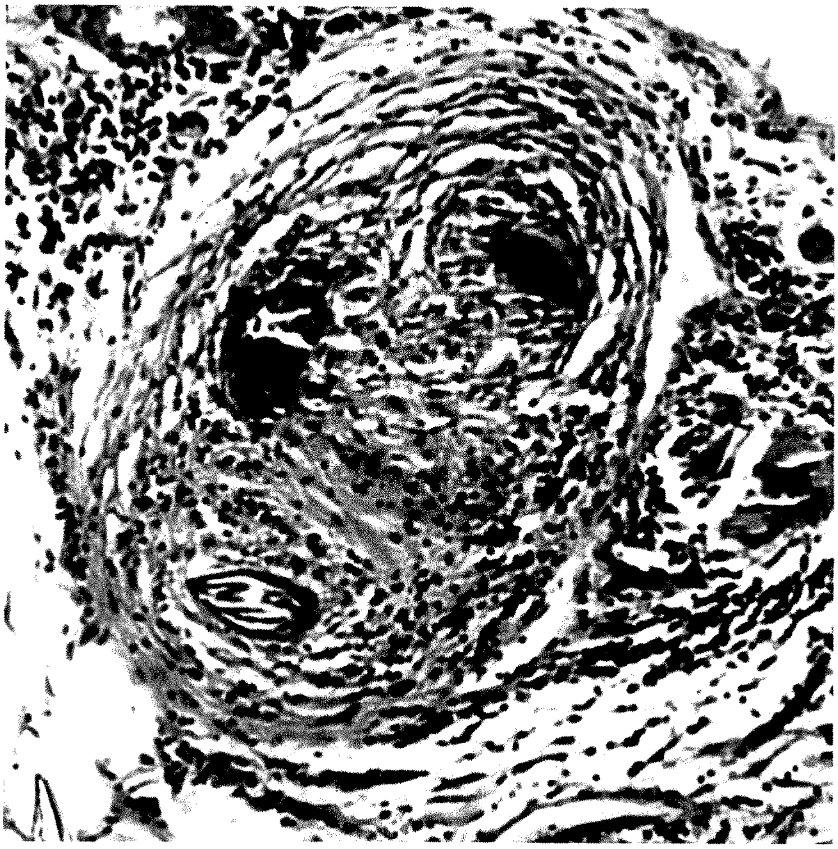


Fig. 10. Case iv. Photomicrograph of section of meso-appendix: calcified schistosome ova within a pseudotubercle (hematoxylin and eosin, × 80).

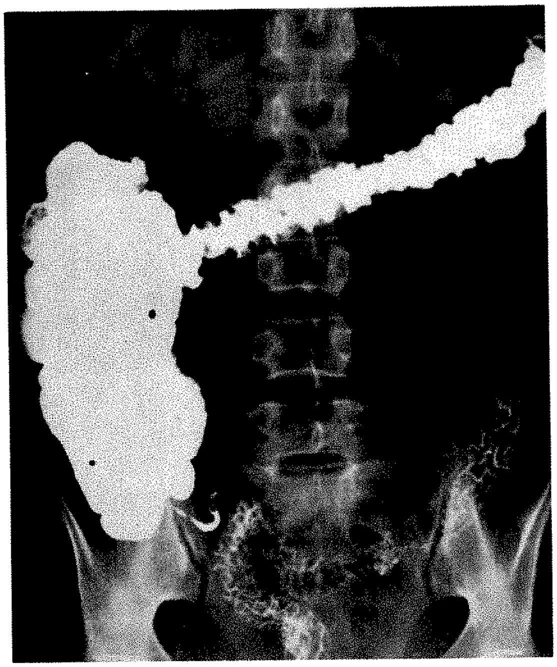


Fig. 11. Case v. Irregularity and spasticity of the transverse colon on filled barium enema study.

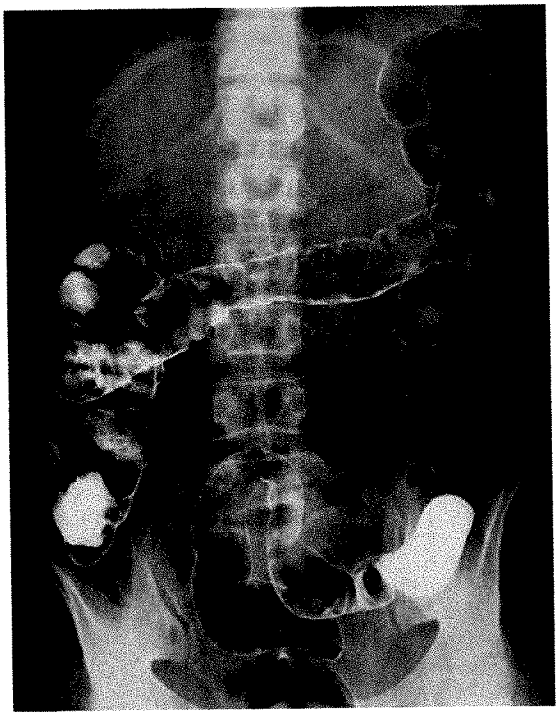


Fig. 12. Case v. Air contrast of the colon during the same examination as in Figure 11 showing incomplete distention of the transverse colon and rigidity of its inferior aspect.

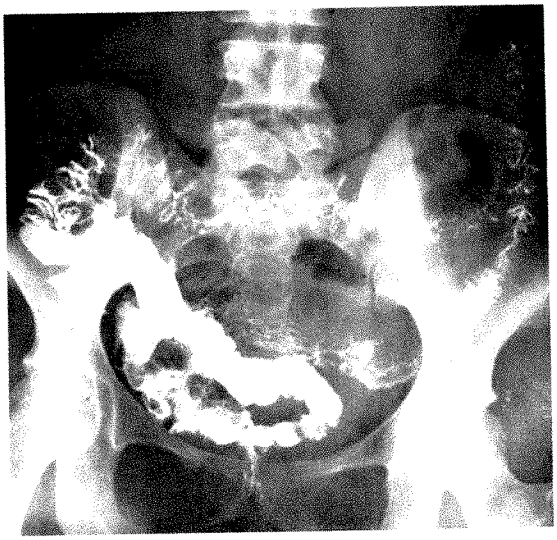


Fig. 13. Case vi. Evacuation barium enema roentgenogram showing marked mucosal irregularity and edema, particularly in the descending and sigmoid colon.

tion and segmentary atonia, particularly in the descending colon and rectosigmoid. Our findings have been similar, and in several instances there has been involvement of the proximal colon. Ulcerations were demonstrated in at least 1 case (Fig. 4 and 5). A statement is made in the above report that filling defects due to papillomas are never seen with *S. mansoni* infestation. This is refuted by our own experience as well as by several reported series, including one in which it was noted that 75 per cent of 159 polyps in infected patients contained *S. mansoni* ova.[13]

We have found strictures of the colon to

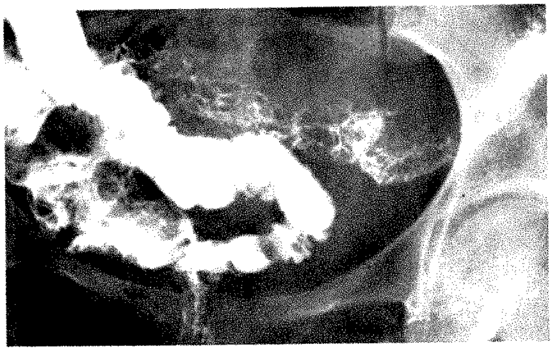


Fig. 14. Case vi. Rectosigmoid colon; detail of Figure 13.

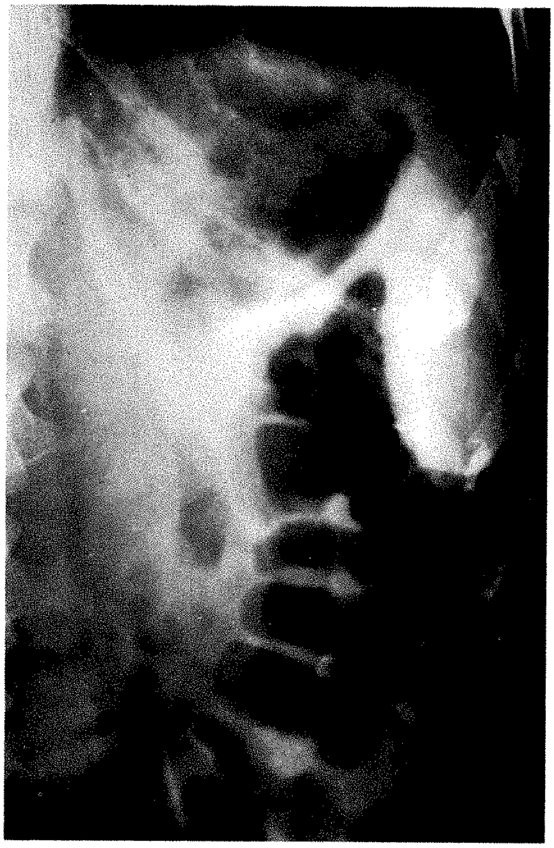


Fig. 15. Case vi. Left upper quadrant of abdomen on March 11, 1959. The spleen does not appear to be enlarged.

be a not uncommon finding (Fig. 2 and 7) and at least 4 patients have been reported elsewhere as being submitted to laparotomy with a preoperative diagnosis of carcinoma of the colon. One of these 4[9] showed a narrowing at the juncture of the descending and sigmoid colon, and an annular constriction was seen on proctoscopy. No ova were found on stool examination. The macroscopic features of the other 3 cases,[43] as well as the roentgenologic signs, resembled those found in neoplasm. The correct diagnoses were made only on histologic examination. There is, parenthetically, no apparent clear-cut relationship between schistosomiasis and carcinoma of the colon[12,37,47] although *S. haematobium* infestation does appear to predispose toward carcinoma of the urinary bladder.[1,47]

Sporadic reports of schistosomiasis of the appendix have appeared,[4,29] in 1 case the serosa being described as studded with small gray sand-like granules, slightly elevated.[25]

II. PORTAL HYPERTENSION

ILLUSTRATIVE CASES

Case vii. P.C., a 33 year old Puerto Rican male (K.C.H. No. 94584), entered the hospital on April 30, 1962, with diarrhea and pruritus ani, epigastric pain and anemia. He had had 3 other admissions over a 3 year period with similar complaints. He was hospitalized 17 years previously in Puerto Rico because of splenomegaly, and was treated for schistosomiasis. Hepatosplenomegaly was found on his more recent hospitalizations, as well as perianal erythema. Sigmoidoscopy to 18 cm. showed no abnormality, but biopsy at 9 cm. was positive for schistosome ova. Eosinophilia on occasion reached levels of more than 60 per cent. A barium enema study showed rigidity and loss of haustrations throughout the descending and sigmoid colon (Fig. 17). Esophageal varices were demonstrated on a barium swallow study (Fig. 18). Splenic pulp pressure was 400 mm. of saline (corrected), normal being 150 to 200 mm. of saline. Splenoportography revealed the presence of extensive collateralization, particularly involving the azygos vein, which was distended and projected to the right of the vertebral col-

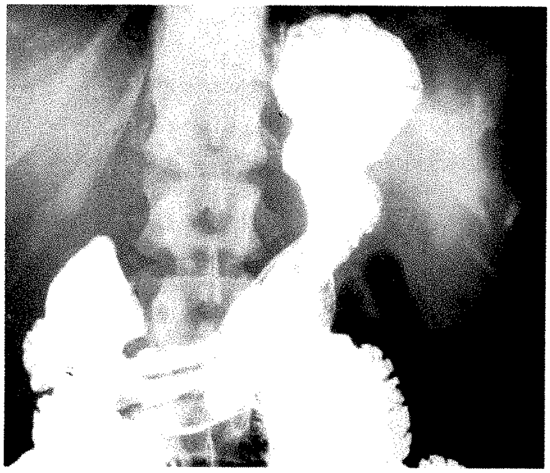


Fig. 16. Case vi. Upper gastrointestinal study of October 25, 1961, showing evident splenomegaly not present 2½ years previously.

umn, presenting roentgenographically as a right retrocardiac soft tissue density. The usual hepatogram was not obtained on late roentgenograms (Fig. 19, 20 and 21).

Case viii. A.C., a 23 year old Puerto Rican male (K.C.H. No. 144474), was admitted on June 8, 1961, with hematemesis and melena. He had had epigastric pain for 3 days previously. His hemoglobin on admission was 5.8 gm. per cent; there was an eosinophilia of 8 per cent. Proctoscopy was negative but rectal biopsy was positive for schistosome ova. Esophageal varices were readily demonstrated on upper gastrointestinal series. The corrected splenic pulp pressure was 270 mm. of saline. Splenoportography showed splenomegaly and numerous collateral vessels, including varices in the gastric fundus (Fig. 22). Following a second proctoscopic examination, the patient developed suprapubic rebound tenderness and the bowel sounds became hypoactive. At laparotomy a sigmoid perforation was found 5 cm. above the rectum, and a transverse colostomy was performed. Upon subsequent colostomy closure, section of the excised portion of the transverse colon showed one schistosome ovum as well as granulomata. A splenorenal shunt was performed some months later. At surgery, portal pressure with the shunt occluded was 280 mm. of saline, and with the shunt patent 240 mm. of saline.

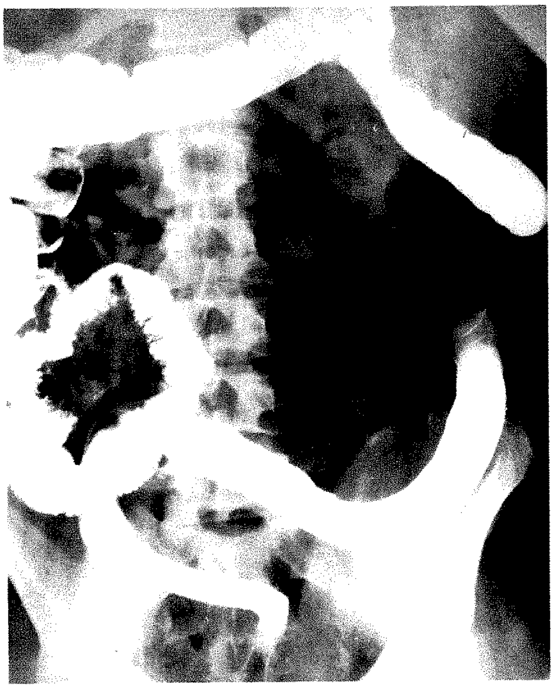


Fig. 17. Case vii. Filled barium enema roentgenogram showing loss of haustration throughout the left hemicolon with narrowing and rigidity.

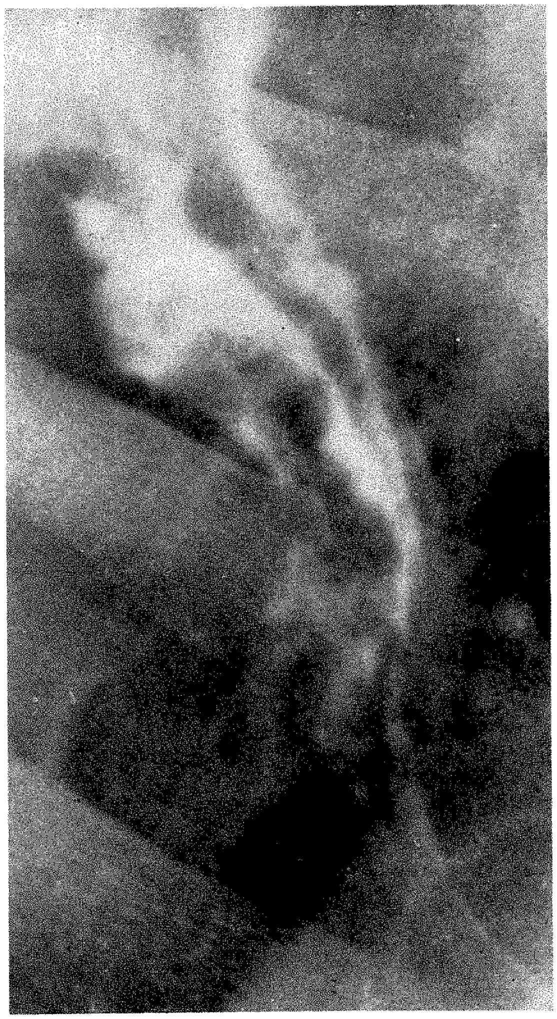


Fig. 18. Case vii. Upper gastrointestinal study showing large esophageal varices.

Case ix. M.A., a 21 year old Puerto Rican female (K.C.H. No. 144571), was admitted on November 30, 1956, with complaints of right upper quadrant pain of 2 days' duration. A cholecystectomy was performed and the pathology report confirmed the surgical impression of chronic cholecystitis. Grossly, the liver appeared cirrhotic. Schistosome ova were found in the liver and appendix. A subsequent T-tube cholangiogram showed crowding and narrowing

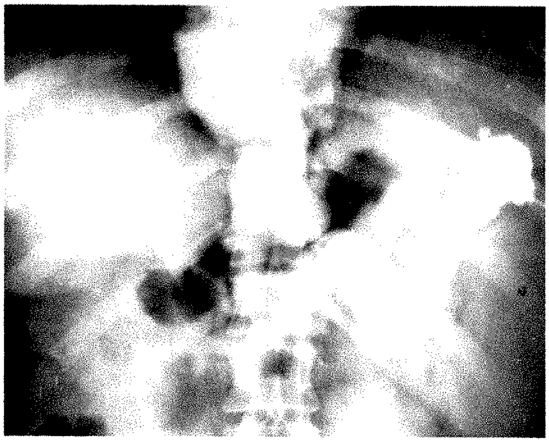


Fig. 19. Case vii. Early splenoportogram showing a large splenic vein and filling of grossly dilated mediastinal collaterals, primarily the azygos and hemiazygos veins.

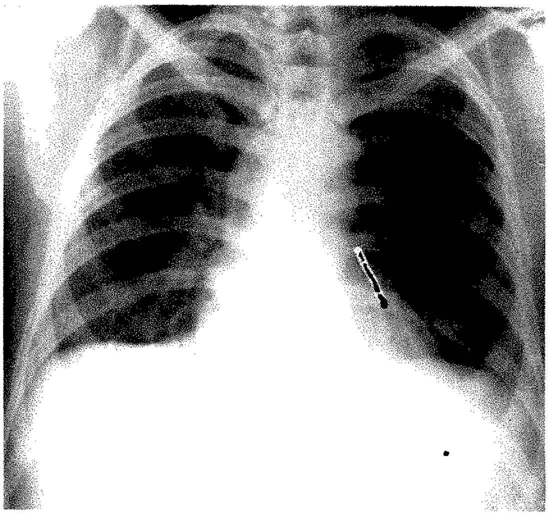


Fig. 21. Case vii. Posteroanterior roentgenogram of the chest showing a right paramediastinal, retrocardiac density representing the dilated collateral veins demonstrated on splenoportography.

of the intrahepatic biliary radicles, creating an arachnoid appearance (Fig. 23).

DISCUSSION

Reports of portal hypertension due to schistosomiasis are frequent. One 26 year old patient suffered 34 episodes of hematemesis before eventually succumbing.[20] Periportal fibrosis of varying degree is said to be encountered, but the hepatic parenchyma is relatively well preserved as compared to Laennec's or postnecrotic cirrhosis.[3,21] Vascular lesions of 3 types are described:[27] (1) substitution by granulomata, (2) sclerosis and narrowing, and (3) intrahepatic thrombophlebitis. Capillary telangiectasis of the portal fields occurs in the most advanced cases. An interesting finding on splenoportography is that as fibrosis proceeds, the intrahepatic ramifications become scarce and the sinusoidal

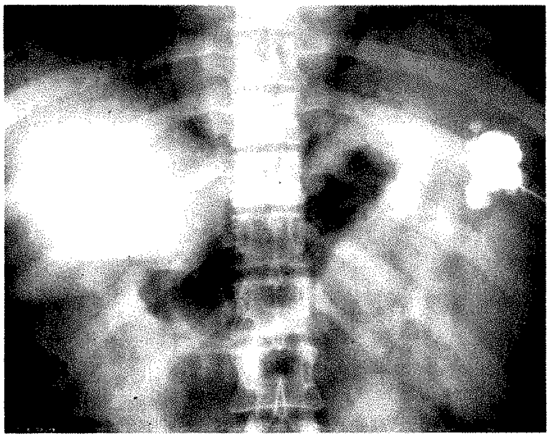


Fig. 20. Case vii. Late splenoportogram. The collateral veins have emptied. A normal hepatogram has not been obtained.

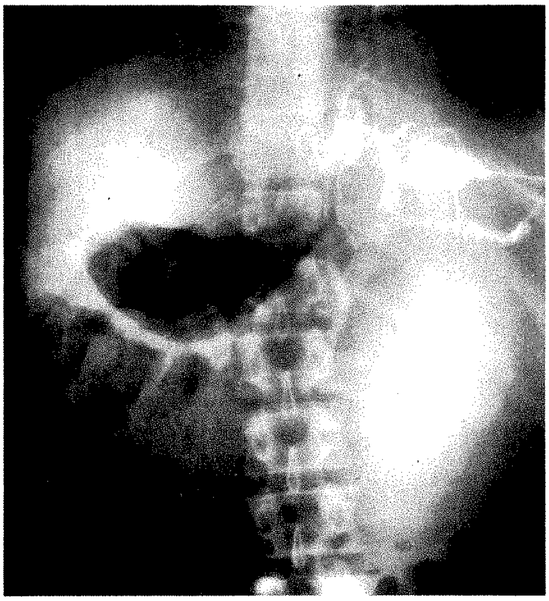


Fig. 22. Case viii. Splenoportogram showing marked splenomegaly and filling of collateral veins in the gastric fundus.

phase becomes fainter with dense patches until it gradually becomes difficult to detect in the terminal stages[40] (Fig. 20).

Portal-systemic shunts of various types have been performed, and, in at least one series, with striking success. Garcia-Palmieri *et al.*[21] report 38 such shunt operations; 33 of their cases had had esophageal bleeding prior to surgery, and none subsequently. They admit the validity of objections to such venous shunts on the grounds that they open a direct channel for the passage of ova from the gastrointestinal tract to the lungs, and so predispose to the development of pulmonary hypertension. Such objections must, of course, be weighed against the dangers of esophageal hemorrhage.

III. PULMONARY AND CARDIAC LESIONS

ILLUSTRATIVE CASES

Case x. E.M., a 13 year old Puerto Rican girl (K.C.H. No. 22174), had been home, febrile, for the 2 weeks preceding admission. She expired shortly following admission, suddenly and unexpectedly, in apparent respiratory distress. At autopsy, schistosome ova and granulomata were found throughout the gastrointestinal tract, in the pancreas, liver, kidneys, and in the thoracic and abdominal lymph nodes. The liver was cirrhotic and the portal vein sclerosed. The spleen was passively congested and ascites was present. Ova and granulomata were present in the lungs, and pulmonary arteriosclerosis and arteriolitis were marked (Fig. 24). The right side of the heart was dilated and hypertrophied.

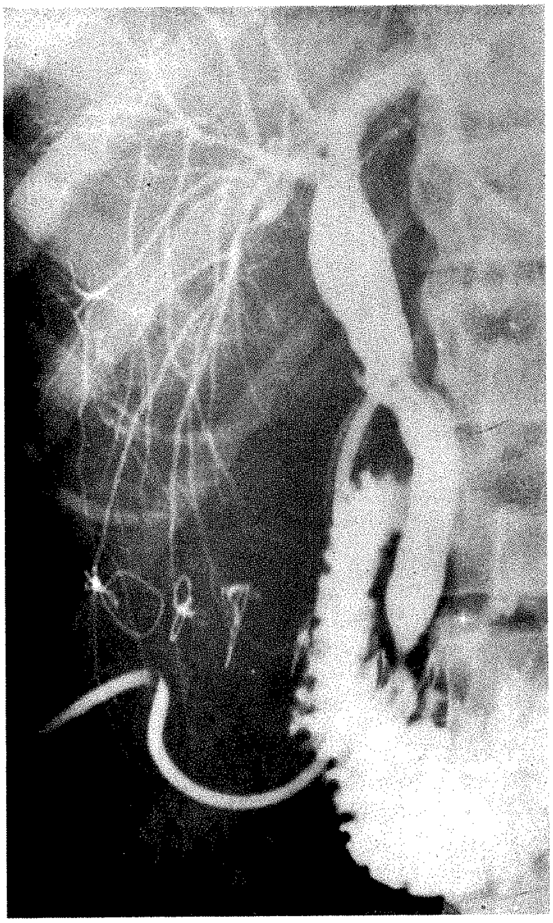


Fig. 23. Case ix. T-tube cholangiogram showing crowding and narrowing of the intrahepatic biliary radicles.

Case xi. J.R., a 24 year old Puerto Rican male (K.C.H. No. 92342), had been admitted on several occasions for "bronchial asthma" which he was said to have had for 10 years. On his last admission, on May 27, 1955, his thorax was noted to be enlarged in its anteroposterior diameter, and inspiratory and expiratory wheezes were heard throughout both lung fields. Eosinophilia was 6 to 8 per cent; vital capacity was 2,000 cc. The electrocardiogram was normal in 1955 and showed right ventricular strain in 1956. No murmurs were heard. A chest roentgenogram in 1955 showed some interstitial fibrosis, but no cardiac enlargement. In 1956, the heart was grossly enlarged and numerous punctate areas of radiodensity were present in both lungs, in addition to the fibrotic changes (Fig. 25 and 26). At autopsy in 1956, left atrial and right ventricular hypertrophy and dilatation were demonstrated and schistosome ova were found in the lungs. The fact that mitral stenosis was also present makes evaluation of the etiology of the chamber enlargement conjectural.

Case xii. W.C., a 30 year old Puerto Rican male (K.C.H. No. 57049), was first admitted to the hospital on October 25, 1962 febrile and complaining of productive cough, chest pain and dyspnea. He had, in fact, been mildly dyspneic and orthopneic for several years. He had been in the United States for 12 years. A diagnosis of right lower lobe pneumonia was made and he was treated with good clinical response. Chest roentgenograms consistently showed prominence of the left heart border in the region of the pulmonary artery (Fig. 27). Electrocardiograms were interpreted as showing right ventricular hypertrophy and strain. Tests of pulmonary function, including ventilatory tests and determinations of arterial gas content, were normal. A cardiac catheterization showed right ventricular and pulmonary artery systolic pressures elevated to systemic levels (115 and 110 mm. Hg, respectively). No evidence of abnormal shunts was found. The only valvular lesion present was that of relative tricuspid insufficiency demonstrated on angiography. Also demonstrated on angiocardiography were a hypertrophied and dilated right ventricle and an aneurysmally dilated pulmonary artery (Fig. 28 and 29). Because of the patient's background, a diagnosis of cor pulmonale on the basis of schistosomiasis was strongly considered, but rectal and liver biopsies remained negative. At this point, the patient signed his release from the hospital against medical advice. This sequence of events was quite similar to that experienced by us in evaluating almost identical findings in Case XIII. In that case, as will be seen, a histologic diagnosis was never made. In the present case, however, the patient returned several days later dyspneic and weak, with paresthesias in both legs. Venous pressure was 330 mm. H_2O and circulation time 17 seconds. He was treated with phlebotomy, digitalis and sedation, but expired the following morning. At autopsy, generalized schistosomiasis was found, with ova in lung, liver, heart, pancreas, colon and kidney. An adult worm was found in a splenic vein. The main pulmonary artery was dilated as suspected and showed diffuse atheromatosis. Arteriolar sclerosis of the smaller vessels was present. The right ventricle was dilated and its myocardium was 0.9 mm thick. The other chambers were of normal size.

Case XIII. I.R., a 21 year old Puerto Rican female (K.C.H. No. 11040), was admitted on March 9, 1962, with epigastric pain and vomiting of 1 day's duration. Similar episodes, accompanied by hematemesis had occurred 3 years prior to admission in Puerto Rico. The spleen was moderately enlarged on physical examination as well as on roentgenograms. Esophageal

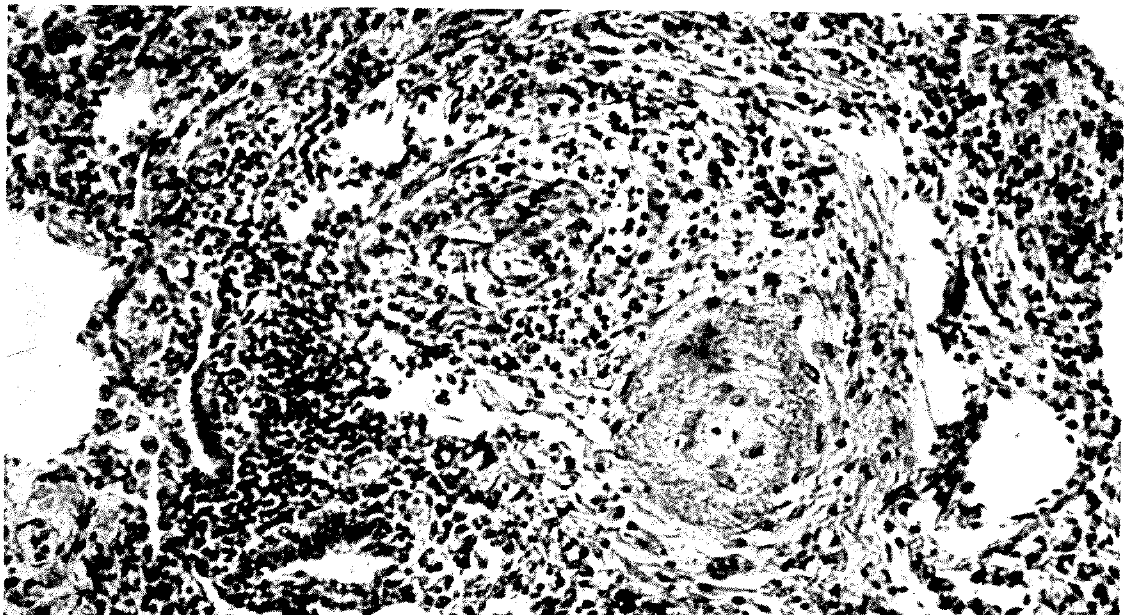


Fig. 24. Case x. Photomicrograph showing pulmonary arteriole markedly narrowed by intimal thickening (hematoxylin and eosin, ×196).

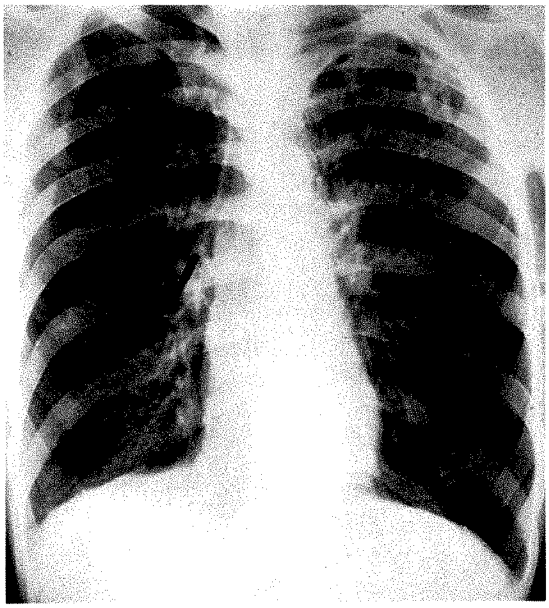


Fig. 25. Case xi. Interstitial pulmonary fibrosis without cardiomegaly: May 31, 1955.

varices were demonstrated on barium swallow study. A diastolic thrill was felt to the left of the sternum. A high-pitched blowing apical early diastolic murmur and a low-pitched loud rumbling mid-diastolic murmur were heard at the left sternal border. Phonocardiogram showed a split second sound with an early and late murmur in diastole. The electrocardiographic find-

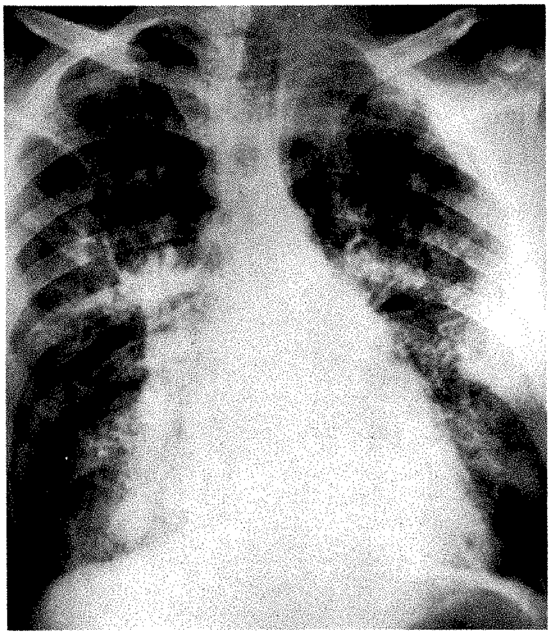


Fig. 26. Case xi. Cardiomegaly, interstitial fibrosis and pulmonary parenchymal nodulations: May 14, 1956.

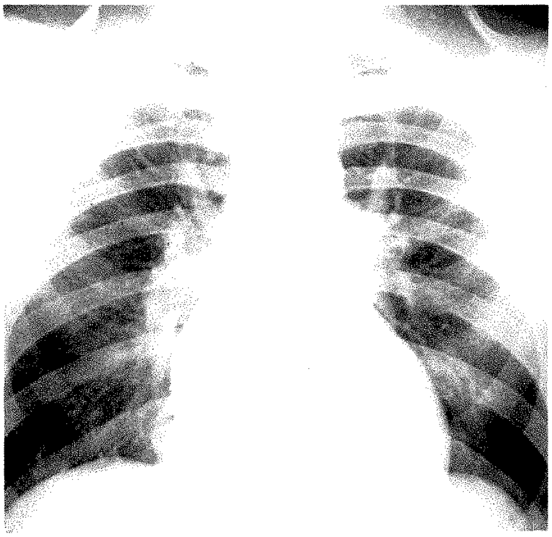


Fig. 27. Case xii. Roentgenogram of the chest demonstrating prominence of the left upper heart border formed by a markedly enlarged main pulmonary artery. The massive hilar shadows are formed by enlarged left and right pulmonary artery branches. Note the rapid peripheral arterial tapering.

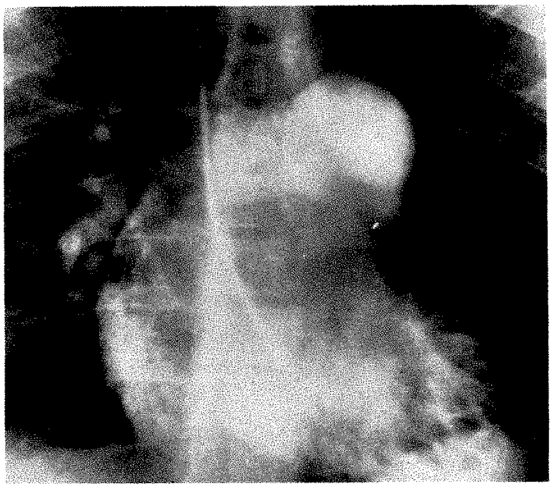


Fig. 28. Case xii. Early anteroposterior roentgenogram of the chest made during selective angiocardiography. The tip of the catheter lies in the inflow tract of the right ventricle. This chamber is hypertrophied and dilated and shows extensive trabeculation. The impression of enlargement of the pulmonary artery gained from Figure 27 is confirmed.

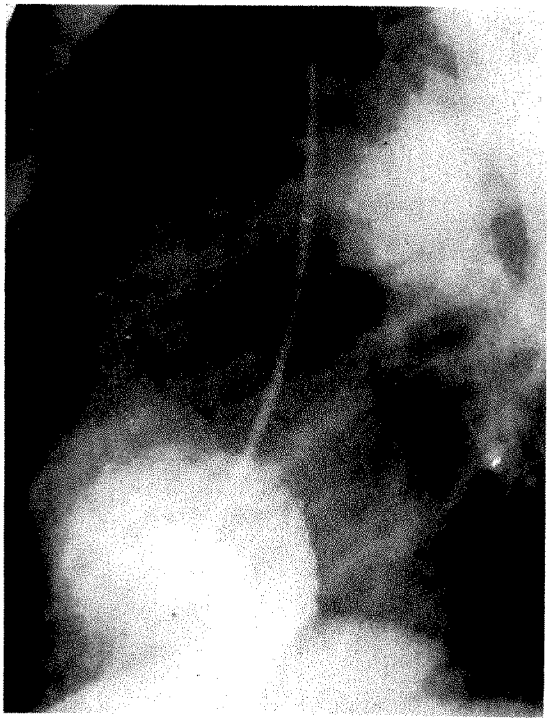


Fig. 29. Case xii. Lateral roentgenogram of the chest exposed simultaneously with Figure 28. The large central pulmonary arteries and abruptly tapering peripheral pulmonary arteries bear a striking similarity to Figure 31.

ings were those of pulmonic insufficiency and pulmonary hypertension with right axis deviation. On cardiac catheterization, no intracardiac shunts were present and no valvular lesions were found. The right ventricular pressure was markedly elevated (systolic 120 mm. Hg and end-diastolic 22 mm. Hg) and the right atrial mean pressure was 12 mm. Hg. Based on these studies, a diagnosis of pulmonary hypertension was made. Chest roentgenograms as well as angiocardiograms showed aneurysmal dilatation of the pulmonary artery as well as rapid tapering of the peripheral pulmonary arteries (Fig. 30 and 31). The patient signed her release from the hospital before further work-up could be accomplished, and a histologic diagnosis of schistosomiasis was not made. We believe, however, the clinical evidence to be compelling on the grounds of splenomegaly, esophageal varices and pulmonary hypertension with aneurysmal dilatation of the pulmonary artery in a young Puerto Rican.

Case xiv. A.V., a 24 year old Puerto Rican female (K.C.H. No. 48090), was admitted with a chief complaint of abdominal pain. She had had right upper quadrant pain, dyspnea and anorexia and had lost 10 pounds in the 4 week period preceding admission. The patient had been in the United States for 7 months. Hepatomegaly was apparent on physical examination. Eosinophilia ranged from 6 to 12 per cent. Schistosome and hookworm ova were present in the stool. A chest roentgenogram showed a massive mediastinal shadow and bilateral pleural effusion (Fig. 32). A pericardiocentesis yielded 320 cc. of straw-colored fluid. At thoracotomy, multiple nodularities were felt in the lungs and there were superficial fibrous plaques. The pericardium was greatly thickened, and the surgical impression was that it was involved by tumor, probably metastatic carcinoma. The pericardial sac was evacuated and a partial pericardiectomy performed. The histologic report was one of granulomatosis involving the lung and pericardium, and pulmonary arteriolitis—findings consistent with schistosomiasis. Cytologic and bacteriologic studies of the surgical specimens and pericardial fluid were negative for malignancy or tuberculosis. On subsequent admissions, numerous thoracenteses were required for reaccumulating pleural effusions.

DISCUSSION

The symptoms of the pulmonary stage of this disease are dyspnea on exertion, general weakness, cough, giddiness and syn-

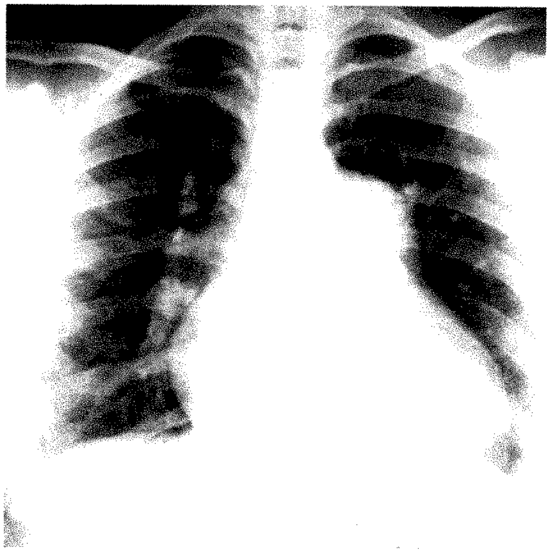


Fig. 30. Case xiii. Marked enlargement of the pulmonary artery. Both lung fields appear normal.

cope, palpitations, thoracic and precordial pain, hemoptysis and other signs of pulmonary hypertension.[15] Vascular lesions include proliferative and necrotizing arteritis, intimal proliferation, thrombosis, and medial and adventitial thickening. Intravascular granulomata, in addition to pulmonary parenchymal granulomata, have been described. These peripheral vascular lesions lead to pulmonary arterial dilatation which may reach aneurysmal proportions[8,15] with right ventricular hypertrophy (Fig. 27–31), and frequently with pulmonic regurgitation evidenced by prominent hilar pulsations on fluoroscopy. Atheromata in the wall of the pulmonary artery as demonstrated in Case XII have been described.[10] Other possible causes of pulmonary hypertension which have been advanced include mechanical arterial obstruction by ova and worms and a theoretical vasospastic and allergic reaction.[6] Pulmonary arteriovenous fistulae have been described.[16,17]

The roentgenograms are frequently normal[7,38] or may demonstrate tortuous pulmonary arteries with irregular contours or beading. The hilar shadows may be prominent with perihilar fibrocalcific strands with or without scanty miliary nodulations, and there may be dense perivascular mottling. Generalized miliary infiltration has been

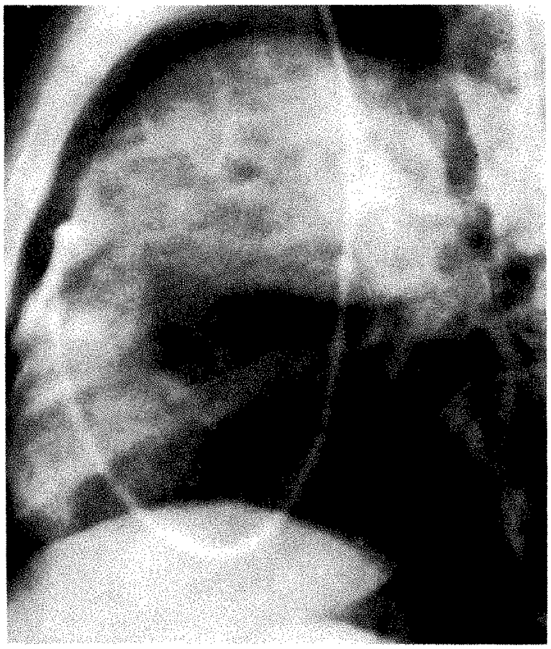


Fig. 31. Case XIII. Lateral roentgenogram of chest made during selective angiocardiography. The tip of the catheter is just below a markedly enlarged pulmonary artery. The peripheral pulmonary arteries taper abruptly.

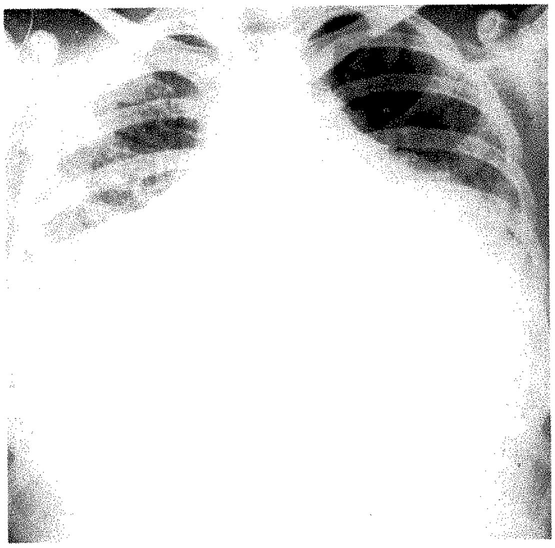


Fig. 32. Case XIV. Massive pericardial effusion and small bilateral pleural effusions, prior to thoracotomy.

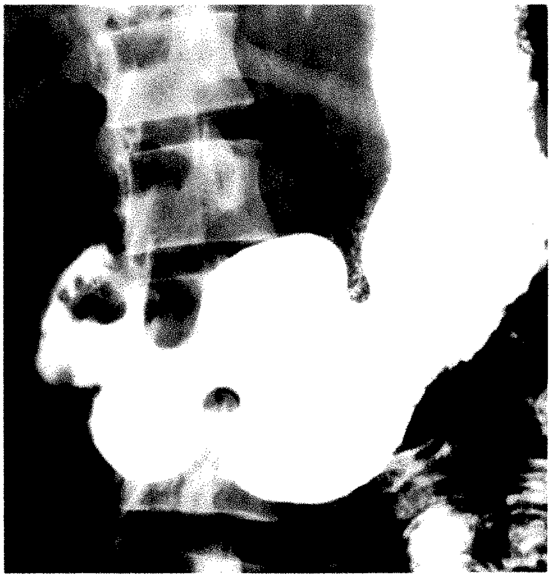


Fig. 33. Case XV. Upper gastrointestinal study showing duodenal deformity; on no obliquity could the second portion of the duodenum be separated from the gastric antrum.

described,[28,42] and the changes have been compared with those of tuberculosis; indeed, the two diseases have been reported concomitantly in the same patient.[33] Our own series includes several patients with pulmonary schistosomiasis and active tuberculosis. The bronchopulmonary phase, as opposed to the vascular manifestations, can progress to bronchitis and emphysema.[24,31,38] That parenchymal granulomata are not frequently found, however, is attested by the fact that in one mass roentgenographic survey in an endemic area, the incidence of pulmonary parenchymal shadows was comparable in infected and noninfected subjects.[39] Miliary nodulation occurring during treatment with antimony is regarded as an allergic reaction about the ova.[14,31]

IV. SMALL BOWEL LESIONS

ILLUSTRATIVE CASES

CASE XV. R.M., a poorly nourished 22 year old Puerto Rican male (K.C.H. No. 91340), was admitted on March 1, 1960, with epigastric distress and persistent vomiting. These complaints had been present in varying degrees for 4 years, and he had lost 35 pounds in the several months preceding admission. He had been told in his youth of having schistosomiasis. On hospitalization elsewhere, 1 year previously, an irritable colon had been diagnosed. At that time, as well as on the Kings County Hospital admission, a deformed duodenal bulb was demonstrated on an upper gastrointestinal study, and on no obliquity could the second portion of the duodenum be separated from the gastric antrum (Fig. 33). A subtotal gastrectomy (Billroth II) was performed. At surgery the stomach was markedly dilated. The pylorus was involved in a

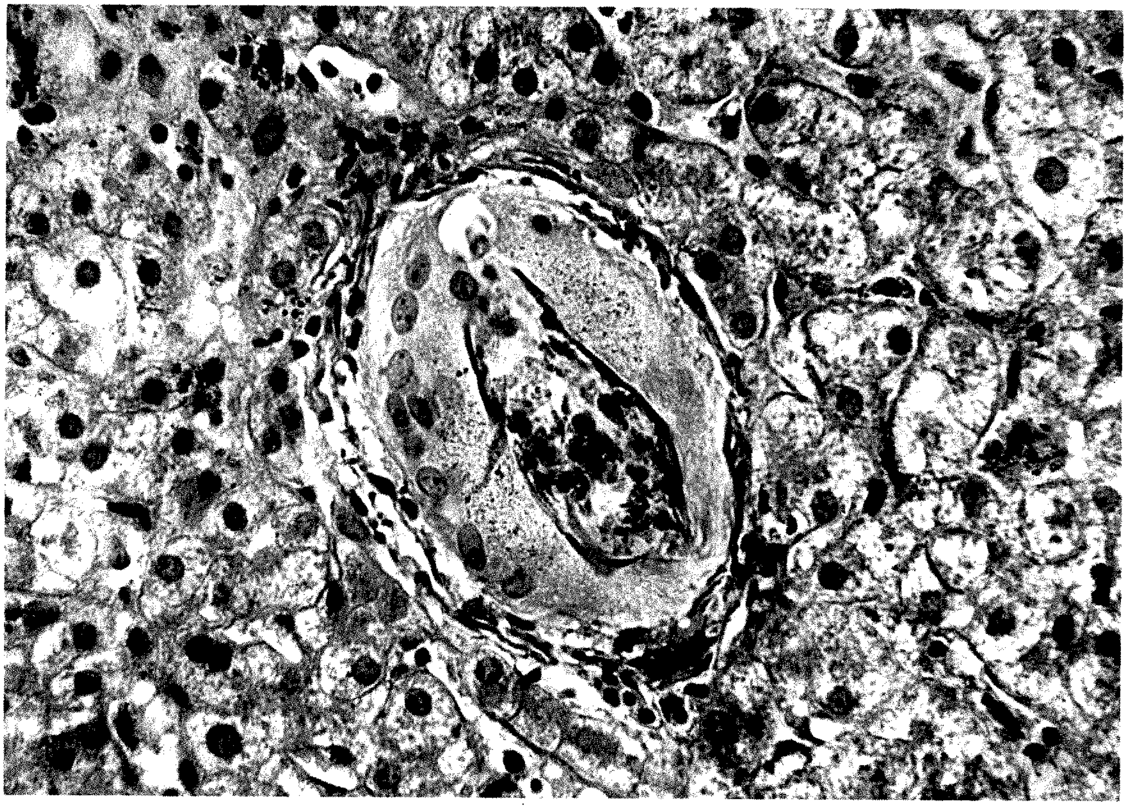


FIG. 34. Case XV. Photomicrograph showing schistosome ovum encased in a large giant cell within a liver sinusoid. Hematin-like pigment is present in the giant cell and in the Kupffer cells (hematoxylin and eosin, ×260).

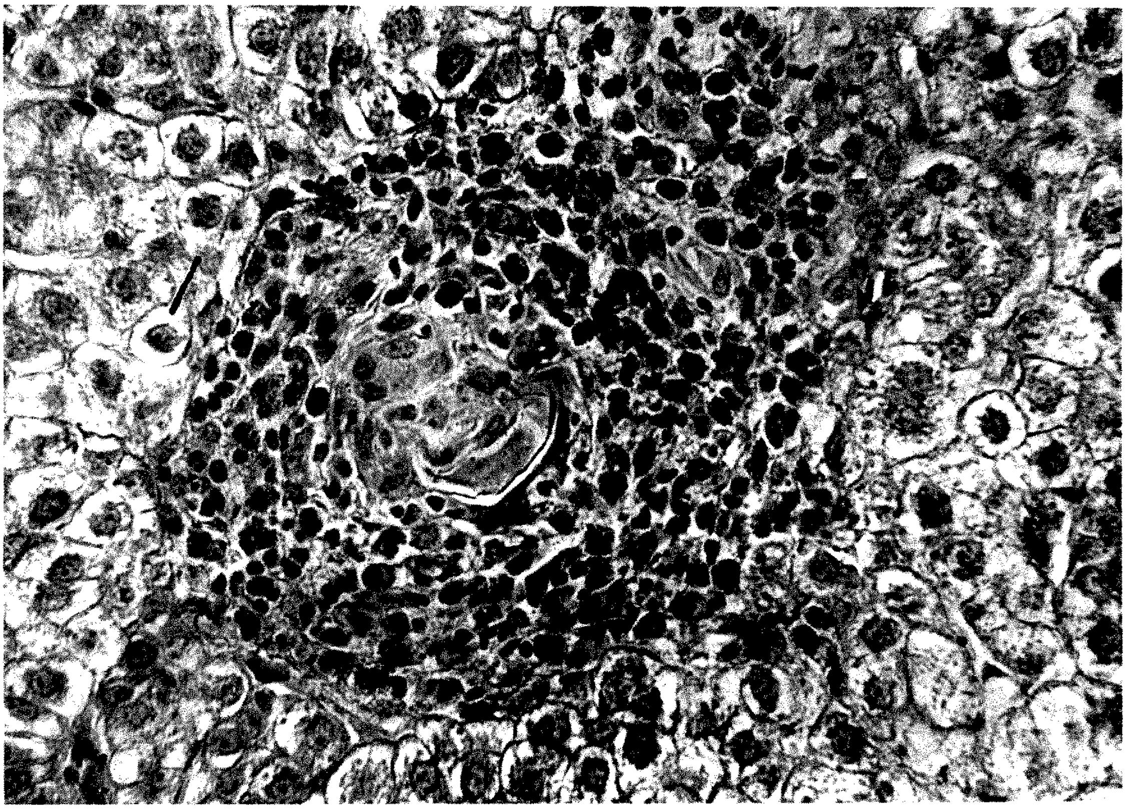


Fig. 35. Case xv. Photomicrograph showing giant cell with cuticle surrounded by myriads of eosinophils in liver (hematoxylin and eosin, ×260).

mass measuring 5×5 cm. in diameter which was adherent posteriorly to the pancreas and involved part of the first portion of the duodenum and prepyloric portion of the stomach along its posterior aspect. No fistulous tract could be demonstrated. There were adhesions of the mass to the fundus of the gallbladder. Several large lymph nodes were found close to the lesion in the lesser sac. At microscopic examination a chronic peptic duodenal ulcer was noted. Schistosome granulomata were demonstrated in the submucosa of the first portion of the duodenum. The omental lymph nodes contained multiple schistosome ova and granulomata, as did the mucosa and submucosa of the appendix. Similar findings were present in the liver (Fig. 34 and 35).

Case xvi. D.V., a 25 year old Puerto Rican male (K.C.H. No. 120937), was admitted on May 5, 1961, with a chief complaint of epigastric pain. Proctoscopy to 15 cm. showed a friable and injected rectal mucosa with small bleeding areas. Stool examination and rectal biopsy were both positive for schistosome ova. A small bowel study (Fig. 36) showed dilatation of loops of jejunum, mucosal edema, and flocculation of barium.

DISCUSSION

Small bowel lesions in schistosomiasis have been infrequently described. They are apparently more often encountered in infestation with *S. japonicum* than with *S. mansoni*. Wang and Kuo[44] have reported 24 cases of small bowel involvement in schistosomiasis japonicum varying in age from 18 to 45 years. They describe coarsening and irregularity of mucosal folds, especially in the upper jejunum, and occasional absence of mucosal folds. There may be flocculation of barium. Also described are abnormalities in the muscle layer, leading to changes in motility and tonicity. A "deficiency pattern" has been described by

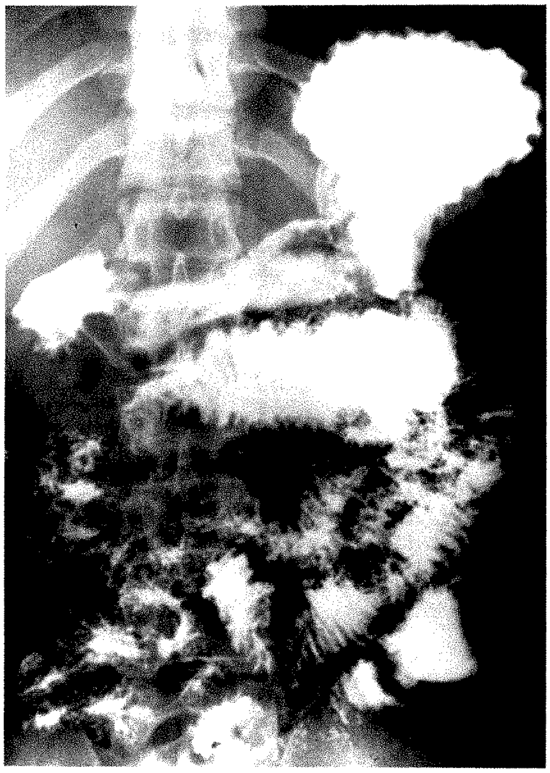


Fig. 36. Case xvi. Early small bowel study showing dilated loops of jejunum and mucosal edema.

Hernandez Morales and Ruiz Cestero.[23] Golden[22] points out that changes found in the small bowel of patients with schistosomiasis cannot with certainty be ascribed to this parasite since multiple infestation is the rule.

V. SKELETAL CHANGES

None of our patients demonstrated skeletal changes such as those described by Pang-Fu and Shao-Chi[32] in patients with schistosomiasis japonicum. In their 12 cases they report bone changes consistent with hypogonadism. They found delayed closure of epiphyses, fine trabeculation, thin cortices, roughened metaphyseal margins and decreased calcification. Although skull sizes were smaller than normal, there was normal closure of sutures, and the sellae turcicae were normal. The ossification centers matured normally, but there was reduction in the length and width of the long bones. Funnel-shaped pelves were found in the females. All of their patients were dwarfed, and it was postulated that both the growth and gonadotrophic hormones were affected.

SUMMARY AND CONCLUSIONS

Schistosomiasis is a disease that has recently assumed great clinical importance in an area in which it had not long ago been a medical oddity. We have presented illustrative material gathered in a relatively short period of time in a hospital in a nonendemic locale, and have reviewed some of the voluminous literature from endemic regions.

None of the roentgenologic changes described in this paper are in themselves pathognomonic for schistosomiasis. The colonic lesions may be mimicked by carcinoma, idiopathic ulcerative colitis, infectious colitis or by other granulomatous colitides. The small bowel changes are also nonspecific. Cirrhosis of any etiology will give approximately the same findings on barium swallow studies or on splenoportography, and splenomegaly is, of course, found in a host of diseases. The difficulty in making a specific roentgenologic diagnosis in disseminated lesions of the lung is well appreciated. We are further well aware that when a disease is as prevalent in a population group as schistosomiasis is in Puerto Rico, there will inevitably be concomitant diseases present that are manifest by changes similar to those of schistosomiasis. We do not deny that idiopathic ulcerative colitis may occur in a patient with schistosomiasis, or that cor pulmonale, unrelated to schistosomiasis, may occur in a patient with proven schistosomiasis. This problem is in many cases difficult or impossible to resolve. However, we believe it a medically responsible conclusion to attribute to schistosomiasis findings compatible with schistosomiasis in a patient proven to be infested with this parasite.

It is our belief that the radiologist is often in the position of being the first to suggest the diagnosis of schistosomiasis provided his index of suspicion is high. We believe that all Puerto Rican patients with vague epigastric distress, portal or pulmonary hypertension, hematemesis or hemoptysis, splenomegaly, esophageal varices, rectal bleeding, roentgen signs of colitis or colonic stenosis, small bowel malabsorption pattern, generalized pulmonary nodulations or fibrosis, right ventricular enlargement, pulmonary artery dilatation and clinical signs of bronchial asthma should be thoroughly investigated for schistosomiasis by repeated stool examinations, rectal, and, if necessary, liver biopsy.

450 Clarkson Avenue
Brooklyn 3, New York

The author wishes to express his gratitude to Drs. Isadore Katz and Henry Burko for reviewing the manuscript, to Dr. Harry Z. Mellins for many helpful suggestions, to Drs. Irving Soifer and Gordon R. Hennigar for review of the illustrative microscopic material, and to Dr. Harold N. Schwinger for permission to use Figure 33.

REFERENCES

1. Ackerman, L. V., and del Regato, J. A. Cancer; diagnosis, treatment and prognosis. Third edition. C. V. Mosby Company, St. Louis, 1962, p. 823.
2. Armbrust, A. F. Rare histopathologic aspects of Manson's schistosomiasis. *Am. J. Trop. Med.*, 1957, *6*, 731–738.
3. Aufses, A. H. Jr., Schaffner, F., Rosenthal, W. S., and Herman, B. E. Portal venous pressure in "pipestem" fibrosis of liver due to schistosomiasis. *Am. J. Med.*, 1959, *27*, 807–810.
4. Baughman, C. H., Michel, M. L., Kuhn, L. J., and Cummins, H. V. Schistosoma japonicum of vermiform appendix and appendices epiploicae. *Am. J. Gastroenterol.*, 1960, *33*, 102–105.
5. Burtner, O. W. Schistosomiasis japonica in American soldiers in Philippines; clinical and laboratory study of 297 treated cases. *J. Philippine M. A.*, 1950, *26*, 537–554.
6. Cavalcanti, I de L., Tompson, G., Souza, N. de, and Barbosa, F. S. Pulmonary hypertension in schistosomiasis. *Brit. Heart J.*, 1962, *24*, 363–371.
7. Chikiamco, P. Schistosomiasis japonica. In: Tropical Radiology. Edited by Middlemiss, H. Intercontinental Medical Book Corporation, New York, 1961, pp. 107–114.
8. Chikiamco, P. S., and Caderao, J. B. Oriental schistosomiasis (Schistosoma japonicum) and certain observable roentgen manifestations. In: International Congress of Radiology. Edited by Rajewsky, B. Urban & Schwarzenberg, Berlin, 1961, pp. 488–489.
9. Cordero, R. L., McCullough, K., Dumeyer, W. H., and Briele, H. A. Schistosomiasis mansoni in Maryland: report of case. *Maryland M. J.*, 1957, *6*, 152–154.
10. Day, H. B. Pulmonary bilharziasis. *Tr. Roy. Soc. Trop. Med. & Hyg.*, 1937, *30*, 575–582.
11. Di Egidio, M. Osservazioni radiologiche sulla bilharziosi intestinale nello Yemen. *Arch. Ital. Sci. Med. Trope., Paras.*, 1957, *38*, 311–327.
12. Dimmette, R. M., Elwi, A. M., and Sproat, H. F. Relationship of schistosomiasis to polyposis and adenocarcinoma of large intestine. *Am. J. Clin. Path.*, 1956, *26*, 266–276.
13. Dimmette, R. M., and Sproat, H. F. Rectosigmoid polyps in schistosomiasis: I. General clinical and pathological considerations. *Am. J. Trop. Med.*, 1955, *4*, 1057–1067.
14. Erfan, H., and Deeb, A. A. Radiological features of chronic pulmonary schistosomiasis. *Brit. J. Radiol.*, 1949, *22*, 638–642.
15. Erfan, M., Erfan, H., Mousa, A. M., and Deeb, A. A. Chronic pulmonary schistosomiasis: clinical and radiological study. *Tr. Roy. Soc. Trop. Med. & Hyg.*, 1949, *42*, 477–485.
16. de Faria, J. L. Pulmonary arteriovenous fistulas and arterial distribution of eggs of *Schistosoma mansoni*. *Am. J. Trop. Med.*, 1956, *5*, 860–862.
17. de Faria, J. L., Barbas, J. V., Fujioka, T., Lion, M. F., Andradre e Silva U. de, and Décourt, L. V. Pulmonary schistosomatic arteriovenous fistulas producing new cyanotic syndrome in Manson's schistosomiasis. *Am. Heart J.*, 1959, *58*, 556–567.
18. Faust, E. C. Inquiry into ectopic lesions in schistosomiasis. *Am. J. Trop. Med.*, 1948, *28*, 175–199.
19. Faust, E. C. Schistosomiasis. In: A Textbook of Medicine. Eighth edition. Edited by Cecil, R. L., and Loeb, R. F. W. B. Saunders Company, Philadelphia, 1951, pp. 410–414.
20. Garcia-Palmieri, M. R., and Marcial-Rojas, R. A. Portal hypertension due to schistosomiasis mansoni. *Am. J. Med.*, 1959, *27*, 811–816.
21. Garcia-Palmieri, M. R., Raffucci, F. L., Díaz-Bonnet, L. A., and Bernal-Rosa, J. F. Shunt surgery for portal hypertension due to *Schistosoma mansoni*; evaluation and management in forty-one cases. *J.A.M.A.*, 1959, *171*, 268–271.
22. Golden, R. Schistosomiasis. In: Radiologic Examination of the Small Intestine. Second edition. Charles C Thomas, Publisher, Springfield, Ill., 1959, pp. 494–497, 500.
23. Hernandez Morales, F., and Ruiz Cestero, G. Roentgenological changes of small intestine

in presence of *Schistosoma mansoni. Puerto Rico J. Pub. Health & Trop. Med.*, 1944, *20*, 507–510.

24. Jawahri, K. I., and Shamma, A. Schistosomal bronchiectasis. *Dis. Chest*, 1960, *38*, 569–571.
25. Koppisch, E. Studies on schistosomiasis mansoni in Puerto Rico. VI. Morbid anatomy of disease as found in Puerto Ricans. *Puerto Rico J. Pub. Health & Trop. Med.*, 1941, *16*, 395–455.
26. Koppisch, E. Diseases due to trematodes. In: Pathology. Edited by Anderson, W. A. D. C. V. Mosby Company, St. Louis, 1948, pp. 417–425.
27. Lichtenberg, F. Lesions of intrahepatic portal radicles in Manson's schistosomiasis. *Am. J. Path.*, 1955, *31*, 757–771.
28. Liu, J., Hsu, C. Y., Hsu, P. Y., and Tai, T. Y. Pulmonary manifestations of acute schistosomiasis japonica. *Chinese M. J.*, 1958, *76*, 144–151.
29. Lovett-Campbell, A. C., and Rose, A. W. Bilharzial appendicitis in *Schistosoma haematobium* infestations; preliminary report. *Tr. Roy. Soc. Trop. Med. & Hyg.*, 1936, *30*, 335–344.
30. Middlemiss, H. Schistosomiasis. In: Tropical Radiology. Edited by Middlemiss, H. Intercontinental Medical Book Corporation, New York, 1961, pp. 98–103.
31. Palmer, P. E. S. Pulmonary manifestations of schistosomiasis. In: Tropical Radiology. Edited by Middlemiss, H. Intercontinental Medical Book Corporation, New York, 1961, pp. 103–107.
32. Pang-Fu, K., and Shao-Chi, C. Observations on skeletal development in schistosomiasis dwarfism. *Nat. Med. J. China*, 1958, *4*, 852–854.
33. Petter, C. K., Morris, K. L., Anawis, E., Dean, G. B., and Fox, D. Concomitant pulmonary schistosomiasis and tuberculosis. *Illinois M. J.*, 1960, *118*, 355–356.
34. Porter, R. J. The human blood flukes. In: Jordan-Burrows Textbook of Bacteriology. Fifteenth edition. Edited by Burrows, W. The W. B. Saunders Company, Philadelphia, 1949, pp. 791–793.
35. Rae, M. V., and Jackson, W. T. Bilharzial appendicitis. *Canad. M. A. J.*, 1960, *82*, 1270–1272.
36. Ragheb, M. Radiological manifestations in bilharziasis. *Brit. J. Radiol.*, 1939, *12*, 21–27.
37. Recio, P. M. Diagnosis and treatment of colorectal schistosomiasis. *Dis. Colon & Rectum*, 1958, *1*, 110–115.
38. Rodríguez, H. F., and Rivera, E. Pulmonary schistosomiasis. *New England J. Med.*, 1958, *258*, 1196–1199.
39. Sami, A. A., Gomaa, T., and El-Alami, M. Parenchymatous (bronchopulmonary) manifestations of pulmonary bilharziasis. *Dis. Chest*, 1960, *38*, 528–532.
40. Semin, R. N. Splenoportography and intrasplenic manometry in hepatic bilharziasis. *Gastroenterologia*, 1960, *93*, 86–106, 167–179.
41. Shookhoff, H. B. Clinical aspects of Manson's schistosomiasis. *New York J. Med.*, 1961, *61*, 3864–3873.
42. Shou-Ho, C., Chung-Ch'i, W., Pao-Ch'ing, W., Ta, K., Yao-teh, C., Chao-ho, C., P'ing-tung, H., and Yuan-fang K. Roentgenological and pathological studies of lungs of rabbits experimentally infected with *Schistosoma japonicum. Chin. J. Radiol.*, 1959, *7*, 81–89.
43. Sobrinho, J., and Kelsch, F. Aspectos tumorais de esquistosomose do colon. *Rev. brasil. radiol.*, 1959, *2*, 1–7.
44. Wang, C., and Kuo, T. Roentgenologic changes of small intestine in schistosomiasis japonica. *Chin. J. Radiol.*, 1958, *6*, 247–253.
45. Warren, L. O., Jr. Asiatic schistosomiasis; report of early case. *New England J. Med.*, 1947, *236*, 24–25.
46. White, P. C., Jr., Pimentel, D., and Garcia, F. C. Distribution and prevalence of human schistosomiasis in Puerto Rico in 1953. *Am. J. Trop. Med.*, 1957, *6*, 715–716.
47. Wu, T. T., Ch'en, T. H., and Chu, C. Relationship of schistosomiasis to carcinoma of large intestine. *Chinese M. J.*, 1960, *80*, 231–242.

Vol. 90, No. 4

THE ROENTGEN FINDINGS IN STRICTURES OF THE COLON ASSOCIATED WITH ULCERATIVE AND GRANULOMATOUS COLITIS*

By RICHARD H. MARSHAK, M.D., CLAUDE BLOCH, M.D., *and*
BERNARD S. WOLF, M.D.
NEW YORK, NEW YORK

STRICTURES of the colon in cases of ulcerative and granulomatous colitis present a problem in differential diagnosis. Although most of these strictures are benign, some represent carcinomas. The present study was undertaken to analyze the roentgen characteristics of benign strictures in patients with ulcerative and granulomatous colitis in an attempt to differentiate them from strictures due to carcinoma. In recent years, we have divided inflammatory disease of the colon into nonspecific ulcerative colitis and granulomatous colitis (Crohn's disease of the colon).[6] This distinction would appear to be important as, up to the present time, strictures occurring in granulomatous colitis have been benign. The term "stricture" is applied to a localized, rigid, filiform narrowing which has produced some antegrade obstruction.

BENIGN STRICTURES IN ULCERATIVE COLITIS

When strict criteria of a stricture are utilized, benign strictures in ulcerative colitis are uncommon. They occurred in 1 per cent of a series of 1,700 cases of ulcerative colitis reviewed for the purpose of this study. The descending colon and ileocecal valve were the usual sites of involvement. In each case where a localized stricture was noted, the remainder of the colon revealed chronic burnt-out ulcerative colitis. In 9 cases, the descending colon was involved and the strictures were typically benign with a concentric lumen, smooth contours and fusiform, convex, pliable, tapering margins. The bowel proximal to the stricture was minimally dilated and on evacuation the colon emptied well (Fig. 1, *A* and *B*). In 2 patients, the lumen of the stricture was slightly eccentric with irregularity of the contours and mucosa simulating a carcinoma (Fig. 2, *A* and *B*). In 1 of these cases, a small sinus tract was demonstrated extending laterally from the distal portion of the stricture (Fig. 3, *A* and *B*). Every patient but one in this series had a localized resection with an end to end anastomosis. Pathologic examination revealed active inflammatory disease at the site of the stricture and immediately proximal and distal to it. Similar findings have been reported by Lumb and Protheroe[5] who studied surgical specimens in 156 cases of ulcerative colitis and found 18 cases with benign strictures. They noted that these strictures occurred either in areas of active ulceration or at the junction of a chronically involved and a relatively normal colon. They made no attempt to differentiate Crohn's disease of the colon from ulcerative colitis.

The genesis of these strictures is unknown but may be due to a healed localized perforation at the site of the markedly inflamed bowel. The postoperative follow-up in this series of cases is of interest. In 2 patients, fistulas formed at the site of the anastomosis which ultimately healed. In 4 patients, there was a postoperative flare-up of the burnt-out ulcerative colitis, necessitating a colectomy and ileostomy. It would appear that if a diagnosis of a benign stricture can definitely be made, conservative treatment is indicated as operation on a colon previously involved with inflammatory disease is frequently followed by complications. All of these cases showed inflammatory changes on pathologic examination and no carcinoma was identified.

---

* From the Department of Radiology, The Mount Sinai Hospital, New York, New York.
Presented at the Sixty-third Annual Meeting of The American Roentgen Ray Society, Washington, D.C., October 2–5, 1962.

A special situation occurred in a case where the right side of the colon was shortened with stricturing of the ileocecal valve and colonization and dilatation of the terminal ileum (Fig. 4, *A* and *B*). The anatomic landmarks were so distorted that the irregular stenotic ileocecal region suggested a carcinoma in the colon. The dilated terminal ileum could easily have been mistaken for a segment of colon and the narrowed ileocecal valve for a carcinoma.

Strictures of the rectum in cases of ulcerative colitis are an ominous finding as they are not infrequently associated with a carcinoma. In this connection, involvement of rectum is much more frequent in ulcerative colitis than in granulomatous colitis. Granulomatous colitis, however, can involve the rectum or any segment of the colon.[9]

BENIGN STRICTURES IN GRANULOMATOUS COLITIS

The coexistence of granulomatous colitis (Crohn's disease of the colon) and ulcerative colitis is undoubtedly possible as we have now observed 4 cases of carcinoma of the small bowel in association with regional enteritis. This combination, however, would appear to be uncommon. Roentgen findings suggestive of granulomatous colitis are: skip areas, longitudinal ulcerations, transverse fissures, eccentric involvement and pseudodiverticula, narrowing with

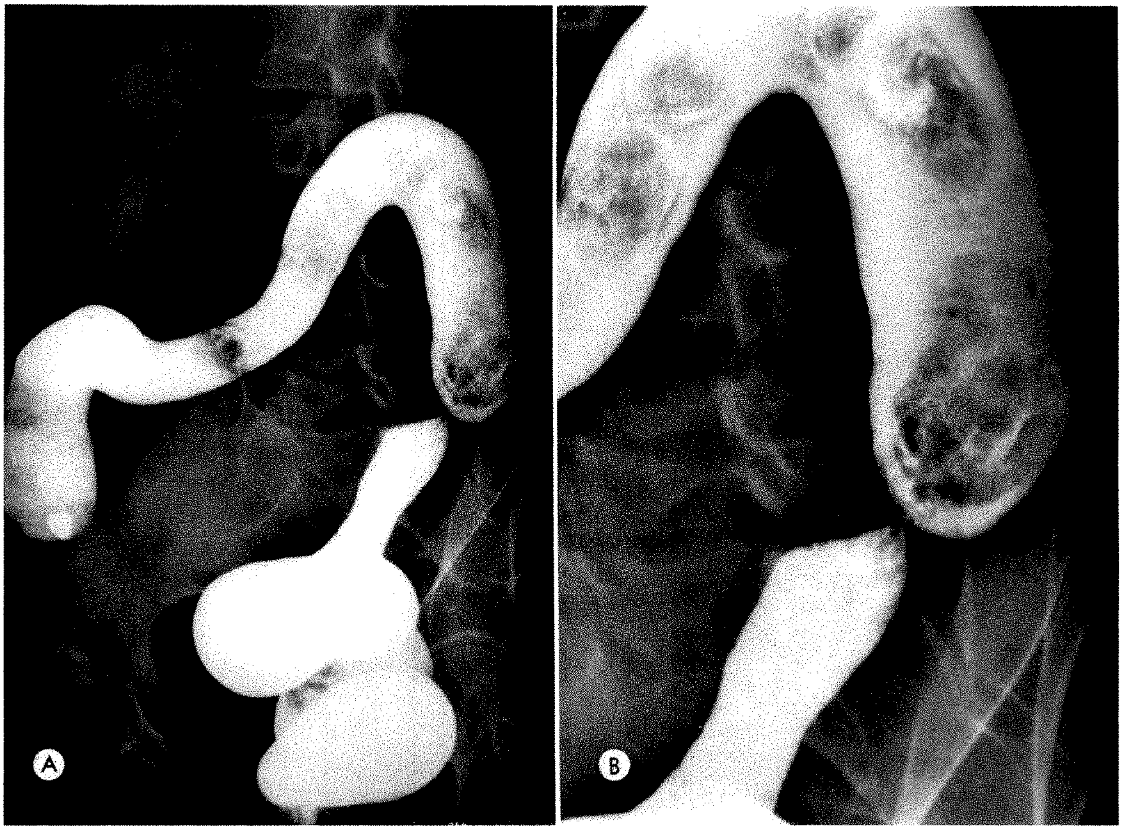


FIG. 1. (*A* and *B*) Roentgenograms show a fusiform tapering stricture with a concentric lumen and smooth contours measuring 1.5 cm. in length in the mid-descending colon. There is a moderate degree of dilatation proximal to the stricture with retained stool and secretions. The entire colon is involved with chronic burnt-out ulcerative colitis. Operative findings: Chronic burnt-out ulcerative colitis with a benign stricture.

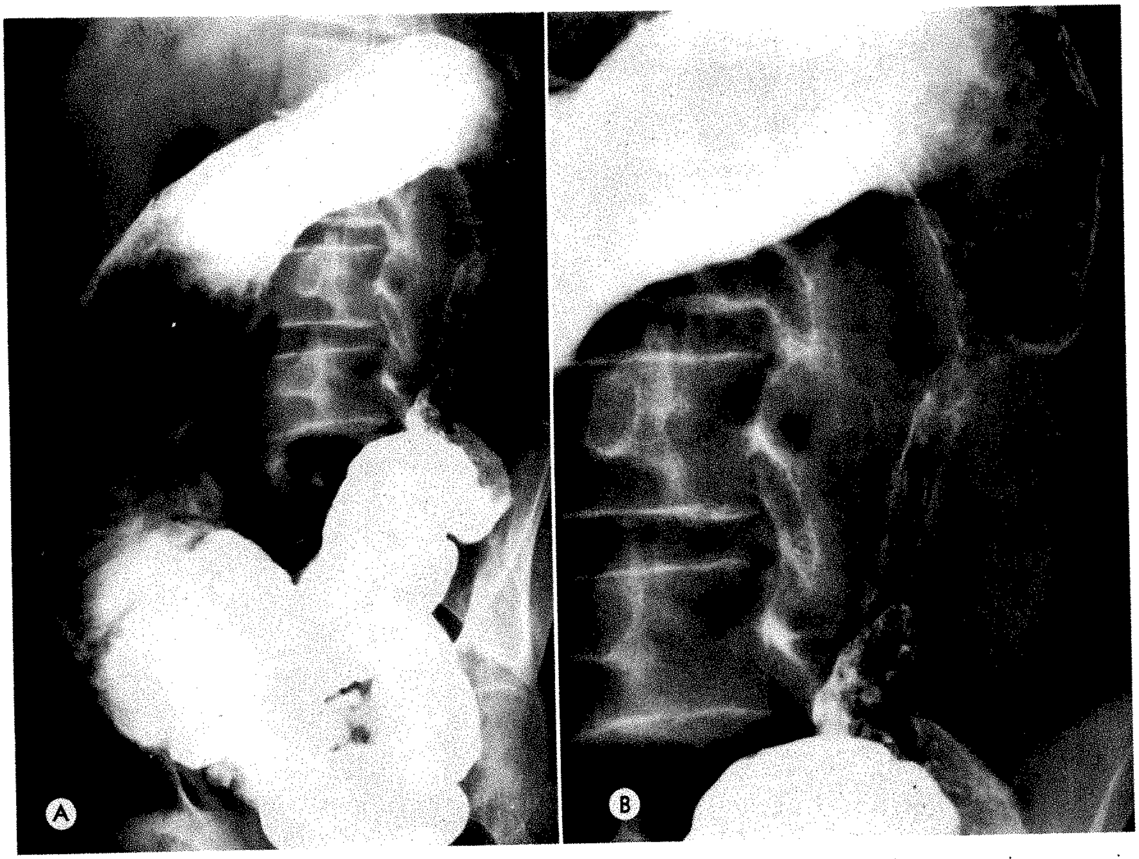


Fig. 2. (*A* and *B*) Roentgenograms show a stricture in the proximal descending colon measuring 4 cm. in length. The lumen is eccentric both proximally and distally with slight irregularity of the contours. There is minimal proximal dilatation. The entire colon is involved with chronic burnt-out ulcerative colitis. Impression: Chronic burnt-out ulcerative colitis with a benign stricture. Follow-up examination 5 years later revealed the entire colon to be markedly shortened. No operation was performed. Such a long segment of narrowing without any of the classic features of a carcinoma favors the diagnosis of a benign process.

rigid walls indicating intramural fibrotic changes, pseudopolypoid changes producing a cobblestone pattern, and internal fistulae. Since marked thickening of the bowel is common in granulomatous colitis, irregular stenotic segments and strictures are frequently seen. In most cases, the lesions are multiple or the roentgen features are typical of a benign stricture and there is no difficulty in making a diagnosis of inflammatory disease (Fig. 5, *A* and *B*). In 6 cases in our series, however, the stenotic segments were single with an eccentric lumen, irregular contours and overhanging margins simulating the appearance of a carcinoma (Fig. 6, *A* and *B*). In these cases, either a segmental colonic resection was performed or an ileosigmoidostomy. In each case, a benign process was present. Follow-up studies revealed normal healing at the anastomosis. This is in contrast to the ulcerative colitis cases where sinus tracts and non-healing were frequent sequelae. This is undoubtedly due to the normal skip areas which are present in cases of granulomatous colitis as contrasted to the diseased bowel found in ulcerative colitis.

After ileosigmoidostomy for regional enteritis or Crohn's disease of the colon, the ileum adjacent to the anastomosis can appear markedly irregular with ulceration

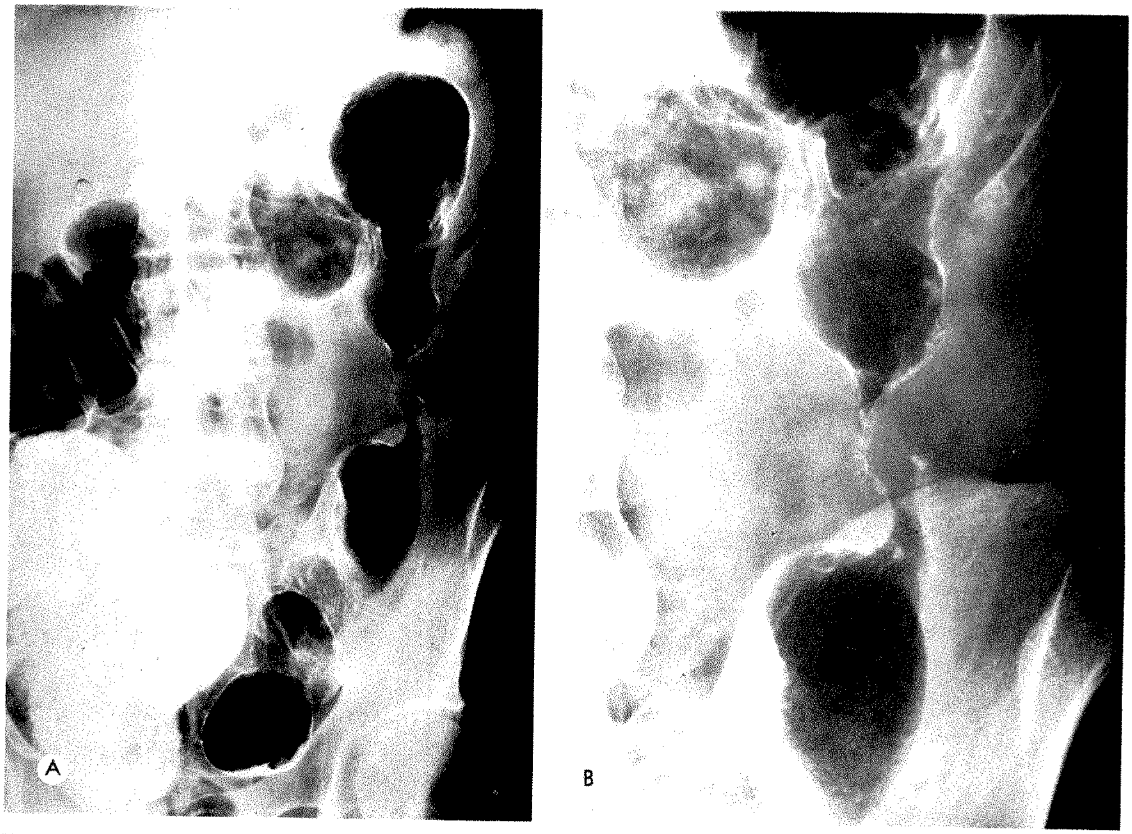
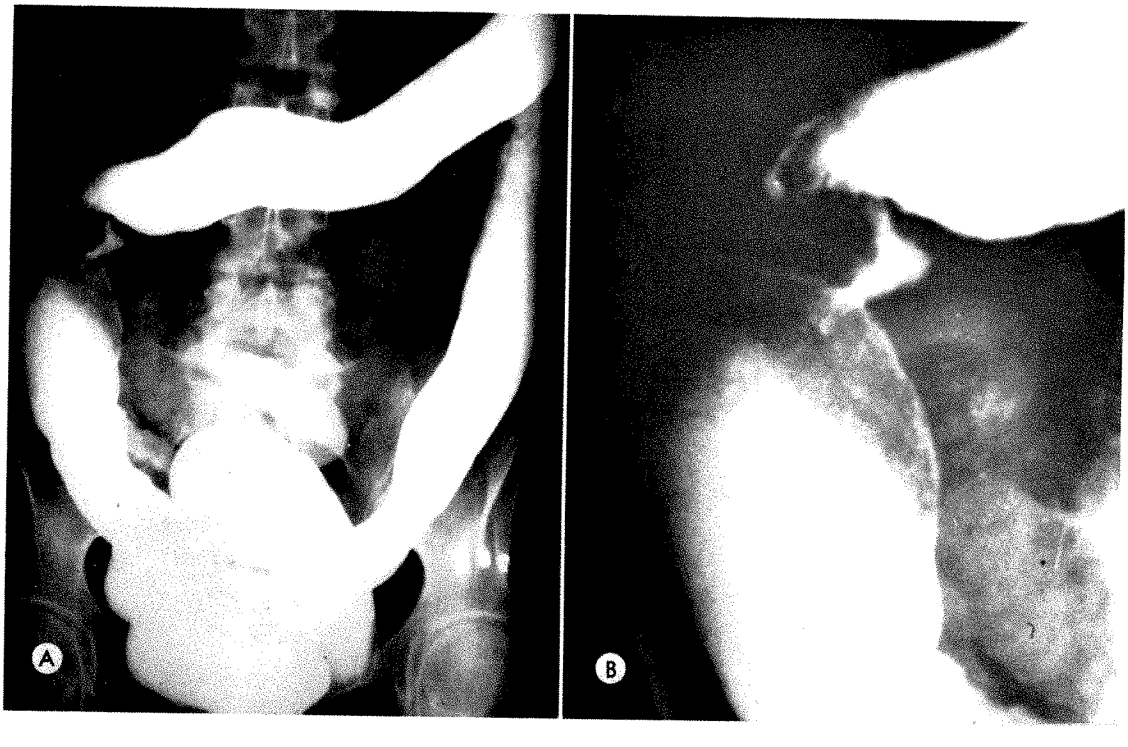


FIG. 3. (*A* and *B*) Roentgenograms show a stricture measuring 3.5 cm. in length in the proximal descending colon. The contours of the stricture are slightly irregular and the lumen is slightly eccentric and angulated. There is a tiny sinus tract extending laterally from the distal portion of the stricture. There is minimal proximal dilatation. The distal half of the colon is involved with chronic burnt-out ulcerative colitis. It was impossible in this case to make a definite diagnosis of a benign or malignant stricture. Operative findings: Pathologic examination revealed a benign stricture.



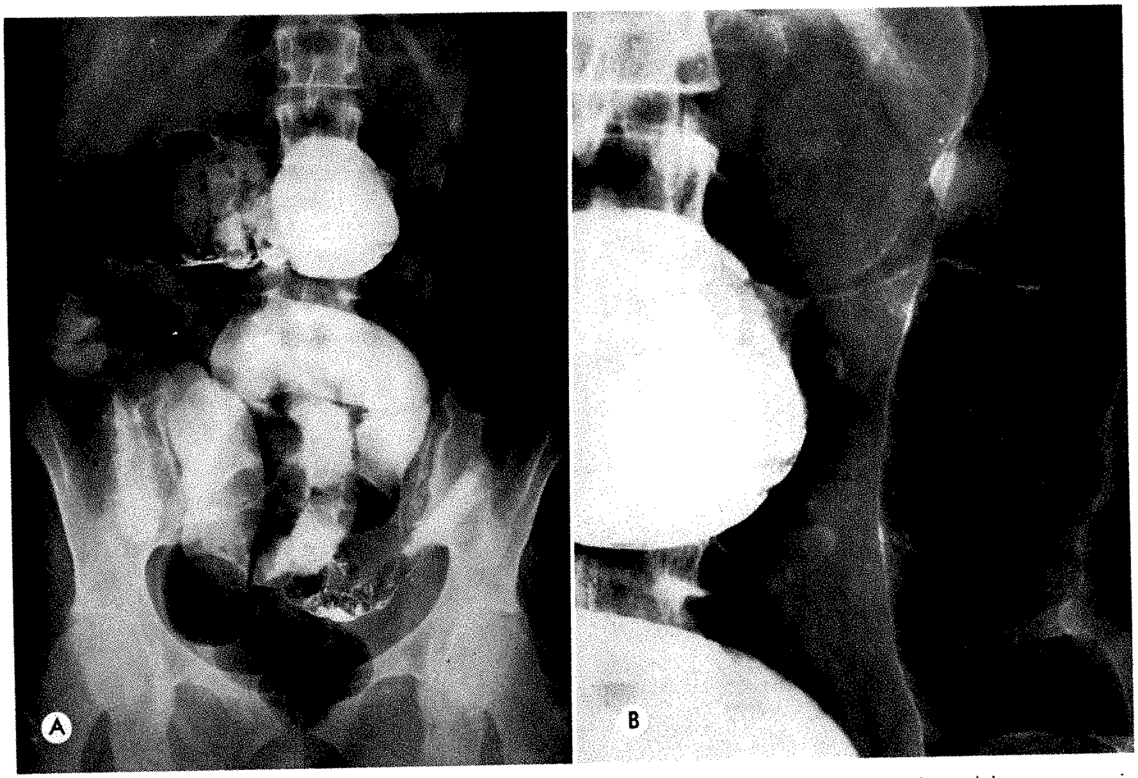


Fig. 5. (*A* and *B*) Roentgenograms show a fusiform stricture in the distal transverse colon with a concentric lumen and sharp margins. There are skip lesions involving the sigmoid, cecum and distal terminal ileum. The remainder of the terminal ileum is dilated. Operative findings: Benign stricture of the transverse colon in granulomatous colitis with a skip lesion in the sigmoid, cecum and distal transverse colon.

of the mucosa and narrowing of the lumen (Fig. 7). Carcinoma in this situation has not been identified and the findings have been due to extension of the inflammatory disease.

CARCINOMAS IN ULCERATIVE COLITIS

Ulcerative colitis associated with a carcinoma was found in 6 per cent of the 1,700 cases studied. In 68 of these patients, the ulcerative colitis was chronic and burnt-out. In 34 cases, the ulcerative colitis was active with evidence of ulceration and inflammatory polyps. In 18 cases, the carcinomas presented as a filiform stricture with none of the usual roentgen characteristics associated with a carcinoma. The roentgen findings were a narrowed segment, usually measuring 2 to 6 cm. in length, with an eccentric lumen, irregular contours and mucosa and flattened, rigid, tapered margins (Fig. 8, *A* and *B*; 9; and 10). There was a moderate degree of dilatation of the proximal bowel with evidence of increased secretions and retained stool. Clinically, symptoms of colonic obstruction were a prominent feature. This is in contrast to benign strictures in ulcerative colitis where, despite marked narrowing, symptoms of obstruction were either minimal or absent.

←

Fig. 4. (*A* and *B*) The right side of the colon is markedly shortened with complete disappearance of the cecum and ascending colon. There is stricturing and irregularity of the ileocecal valve associated with dilatation of the terminal ileum. The failure to recognize the dilated terminal ileum may result in a mistaken diagnosis of a carcinoma. Operative findings: Ulcerative colitis with a stricture at the ileocecal valve.

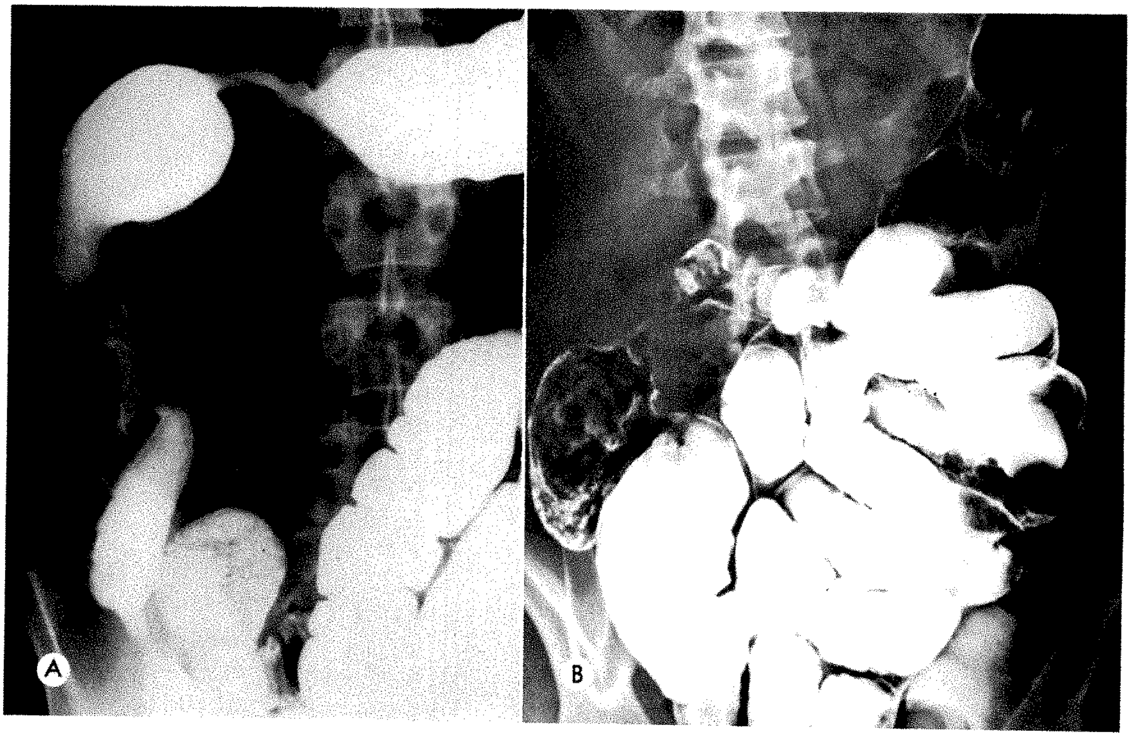


Fig. 6. (*A*) Roentgenogram shows a fusiform concentric narrowing with smooth contours involving the proximal transverse colon. There are skip lesions in the ascending colon, cecum and terminal ileum. Operative findings: Granulomatous enterocolitis with a benign stricture in the proximal transverse colon. (*B*) Roentgenogram shows an irregular stricture with slightly overhanging margins involving the proximal transverse colon. The remainder of the colon is normal. The small bowel is dilated. In this case, it is impossible to exclude a carcinoma. Operative findings: Granulomatous colitis with a benign stricture.

The carcinomatous strictures in this group were found in the distal transverse colon, the left side of the colon and the rectum. The atypical roentgen features were probably due to the underlying inflammatory disease in the affected bowel and the submucosal situation of the carcinomatous tissue. Pathologic study of these cases showed that the deep layers of fibrous tissue were infiltrated by scirrhous carcinoma. In the other cases, the carcinoma, in spite of the underlying ulcerative colitis, had the usual roentgen characteristics associated with a malignancy and presented no problem in differential diagnosis (Fig. 11).

CONCLUSIONS

Strictures, either benign or malignant, are uncommon in cases of ulcerative colitis.

Fig. 7. Status post ileosigmoidostomy for regional enteritis involving the terminal ileum with recurrence at the ileum adjacent to the anastomosis. Roentgenogram shows marked effacement and ulceration of the mucosa with overhanging margins simulating a carcinoma. Operative findings: Recurrent inflammatory disease in the ileum.

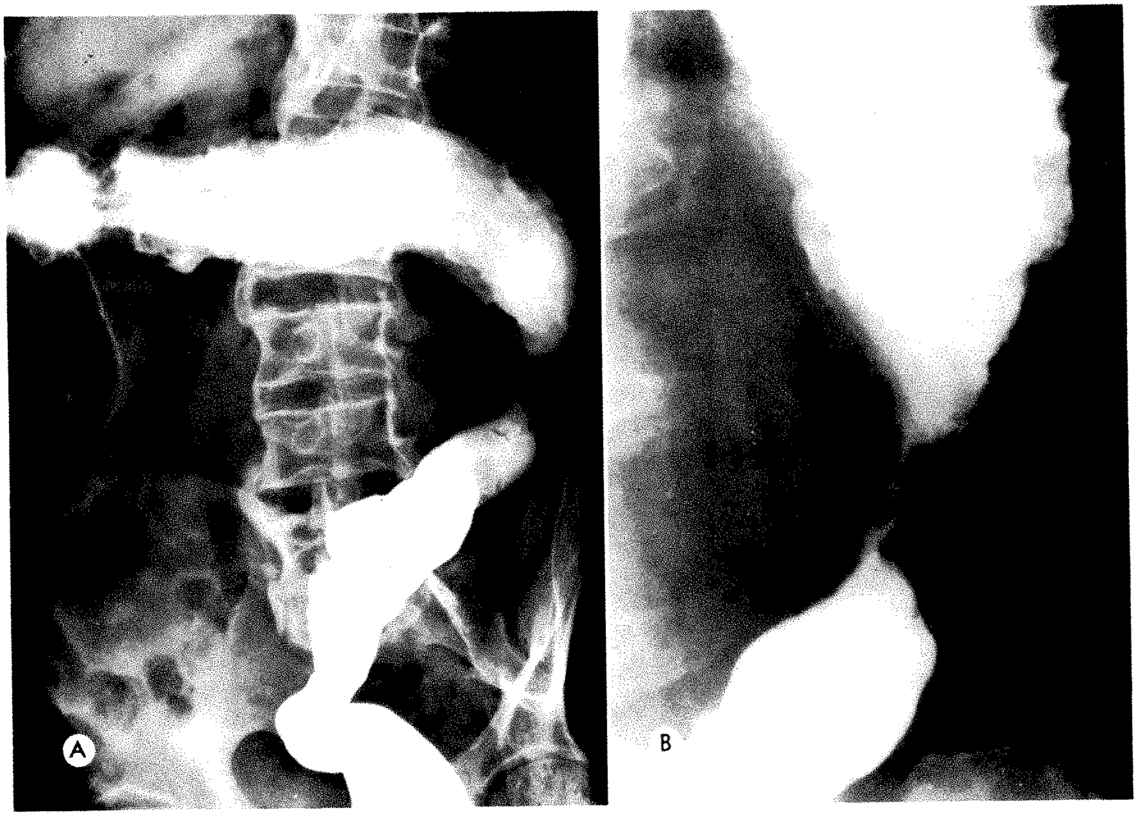


Fig. 8. (*A* and *B*) Carcinomatous stricture involving the proximal descending colon with an eccentric lumen, irregular contours and moderate dilatation of the proximal bowel. The entire colon is involved with burnt-out ulcerative colitis. Operative findings: Carcinomatous stricture with burnt-out ulcerative colitis.

However, this finding can be the sole roentgen evidence indicating the presence of a carcinoma. The present study revealed that when all of the features of a benign stricture are demonstrated, such as a concentric lumen, fusiform tapering margins and smooth contours, a carcinoma is unlikely. When there is any atypism or devia-

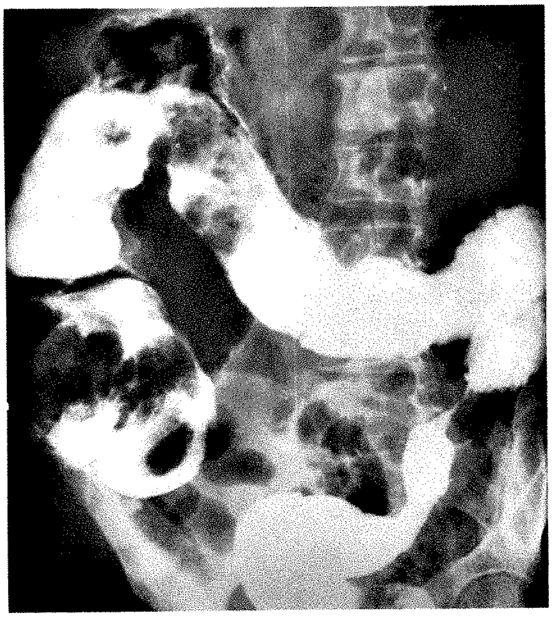


Fig. 9. Carcinomatous stricture involving the proximal descending colon with an eccentric lumen and irregular contours. There is marked dilatation of the proximal bowel and considerable secretion. The entire colon is involved with burnt-out ulcerative colitis. Operative findings: Carcinomatous stricture with burnt-out ulcerative colitis.

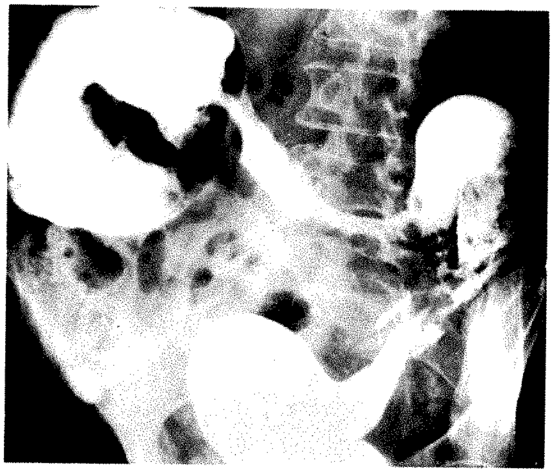


Fig. 10. Roentgenogram shows an irregular stricture involving the proximal descending colon and several fistulous tracts. Operative findings: Carcinomatous stricture with chronic burnt-out ulcerative colitis.

tion from these findings, carcinoma cannot be excluded and exploration should be performed. It is important to note that healing at the anastomotic site is frequently impaired following surgery for strictures associated with chronic burnt-out ulcerative colitis and that, in these cases, a colectomy may be necessary.[4] Localized narrowing of the bowel is more frequent in Crohn's disease of the colon (granulomatous colitis). Up to the present time, no carcinomas have been identified in Crohn's disease of the colon and the differentiation of this entity from ulcerative colitis is therefore important. It should be pointed out, however, that this differentiation is not always possible. Removal of granulomatous strictures is usually followed by an uncomplicated postoperative course, providing the anastomosis is performed through normal bowel.

Richard H. Marshak, M.D.
1075 Park Avenue
New York, New York

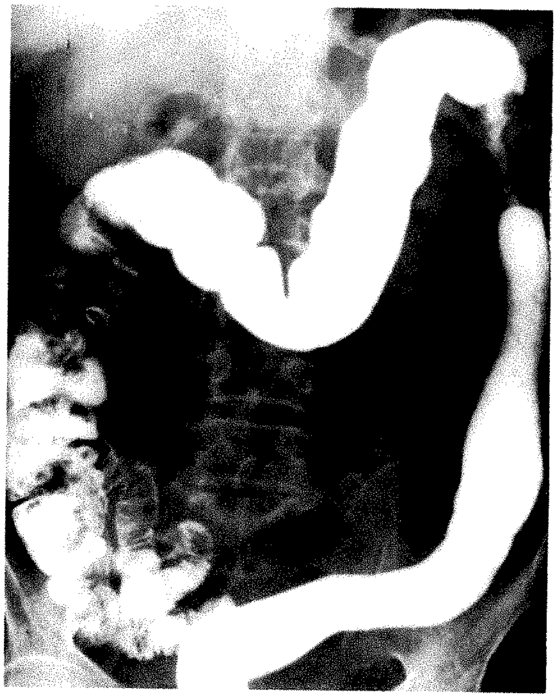


Fig. 11. Carcinoma of the proximal descending colon in a case of chronic burnt-out ulcerative colitis presenting the typical roentgenographic appearance.

REFERENCES

1. Bockus, H. L., Roth, J. L., Buchman, E., Kalser, M., Staub, W. R., Finkelstein, A., and Valdes-Dapena, A. Life history of nonspecific ulcerative colitis: relation of prognosis to anatomical and clinical varieties. *Gastroenterologia*, 1956, *86*, 549–581.
2. Boreham, P. Benign strictures of colon. *Proc. Roy. Soc. Med.*, 1957, *50*, 601–604.
3. Edling, N. P. G., and Eklöf, O. Radiologic findings and prognosis in ulcerative colitis. *Acta chir. scandinav.*, 1961, *121*, 299–308.
4. Hodgson, J. R., and Sauer, W. G. Roentgenologic features of carcinoma in chronic ulcerative colitis. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1961, *86*, 91–96.
5. Lumb, G., and Protheroe, R. H. B. Ulcerative colitis; pathologic study of 152 surgical specimens. *Gastroenterology*, 1958, *34*, 381–407.
6. Marshak, R. H., Wolf, B. S., and Eliasoph, J. Segmental colitis, *Radiology*, 1959, *73*, 707–716.
7. Neuman, H. W., Bargen, J. A., and Judd, E. S., Jr. Clinical study of two hundred one cases of regional (segmental) colitis. *Surg., Gynec. & Obst.*, 1954, *99*, 563–571.
8. Weingarten, B., and Weiss, J. Malignant degeneration in chronic inflammatory disease of the colon and small intestine. *Am. J. Gastroenterol.*, 1960, *33*, 203–207.
9. Wolf, B. S., and Marshak, R. H. Roentgen findings in granulomatous colitis. To be published.

Vol. 90, No. 4

DEMONSTRATION OF FISTULAS BY VAGINOGRAPHY*

By R. W. LAMBIE, M.D.,† S. RUBIN, M.D.,‡ *and* D. S. DANN, M.D.§
KANSAS CITY, MISSOURI

THE roentgen demonstration, identification and localization of vaginal fistulas often present difficult problems. This applies primarily to fistulas which are high in the vaginal vault since rectovaginal fistulas between the distal ends of the rectum and vagina can easily be identified by the passage of probes or with contrast studies. However, in cases of fistulas which are high in the vagina often only the opening in the vaginal vault can be seen and the exact portion of the bowel with which the fistulous tract communicates remains obscure. Proper identification of the fistulous communications is a prerequisite to adequate treatment, inasmuch as the fecal stream must be diverted in many cases before repair is undertaken.

Fistulas between the vagina and intestinal tract may result from congenital malformation, inflammatory process, trauma, obstetric injury, operative trauma, malignant disease and irradiation. The incidence of rectovaginal fistulas has increased somewhat because of the more recent radical treatment of pelvic cancers. This is in part due to the use of higher radiation dosage made possible by supervoltage techniques. Frich[1] has clearly shown in his survey of 748 cases of cancer of the cervix that the incidence of fatalities and severe complications rises markedly when a tumor dose of more than 4,000 r is given in a period of 4 to 6 weeks.

When a patient with fecal drainage from the vagina is sent to the Department of Radiology, a barium enema study is usually requested. It is the purpose of this communication to show that at times rectovaginal fistulas cannot be demonstrated by the conventional barium enema examination. Furthermore, when a fistula to the large bowel is observed on a barium enema study, erroneous conclusions may be reached because other fistulous tracts to the small bowel may also be present but are not demonstrated. The following type of examination is proposed to avoid such errors.

TECHNIQUE FOR VAGINOGRAPHY

A standard rectal enema tip with retention bag is inserted into the lower end of the vagina with the patient in the supine position on the fluoroscopic table. She is instructed to keep her legs together, and under direct fluoroscopic observation the retention bag is inflated. A moderately thin solution of barium sulfate is injected slowly and spot roentgenograms are made as the fistulous tracts are visualized. When the fluoroscopist is satisfied that he has observed all communications, conventional roentgenograms are taken of the general area after which the patient is allowed to expel the barium. A cleansing douche is given at the end of the examination.

The following case reports illustrate the value of direct vaginal administration of barium, as contrasted to the usual barium enema study, in vaginal fistulas.

REPORT OF CASES

CASE I. W.M., a 46 year old Negro female, was admitted to the hospital on April 3, 1961 with a provisional diagnosis of fibroids of the uterus and a right ovarian cyst. At surgery the diagnosis was confirmed but the patient was also found to have an unsuspected severe chronic pelvic inflammatory disease. A total hysterectomy, left salpingo-oophorectomy and right para-ovarian cystectomy were performed with difficulty due to inflammation of the tis-

---

* From the Department of Radiology, Menorah Medical Center, Kansas City, Missouri.

† Resident.

‡ Radiologist.

§ Radiologist-in-Chief.

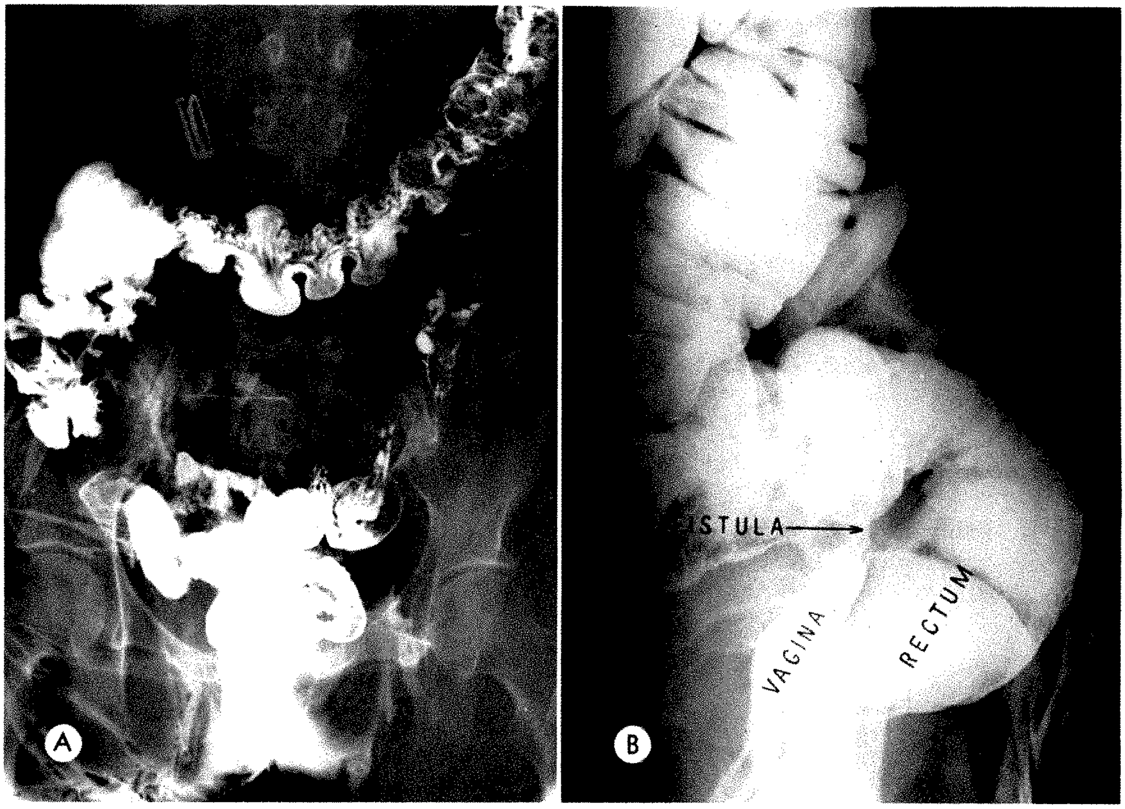
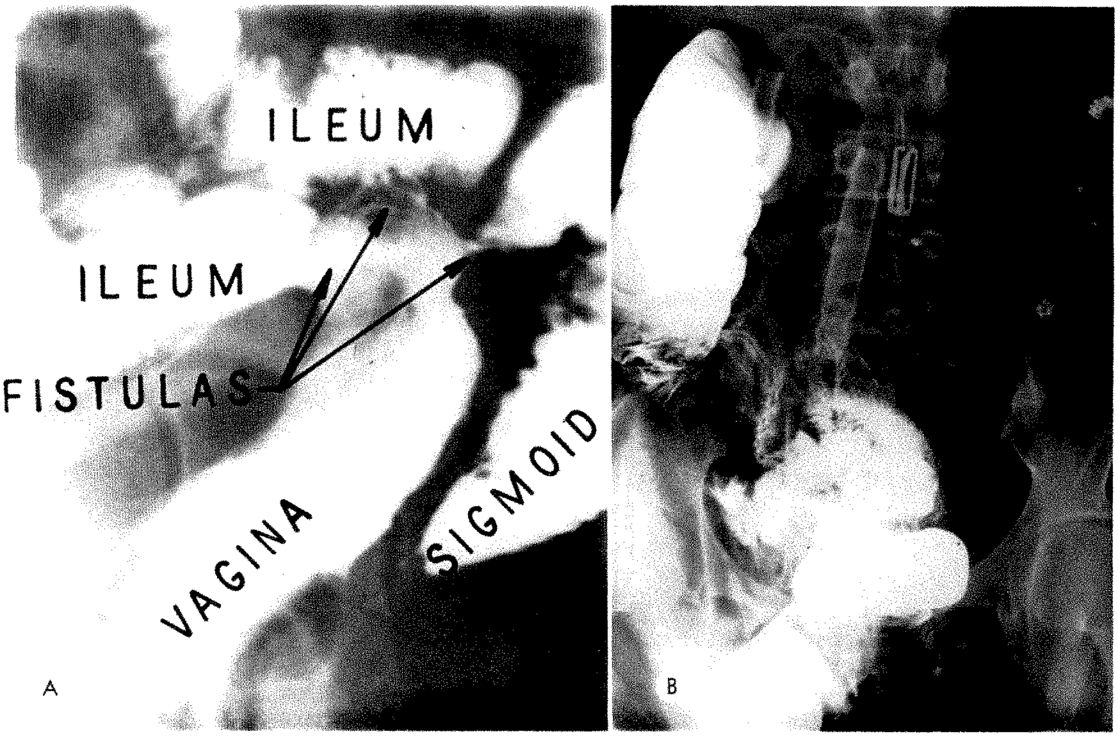


FIG. 1. Case 1. (*A*) Anteroposterior and (*B*) lateral barium enema studies. A single fistulous tract between the vagina and sigmoid is demonstrated. Barium on the table is due to the patient's inability to retain the enema.



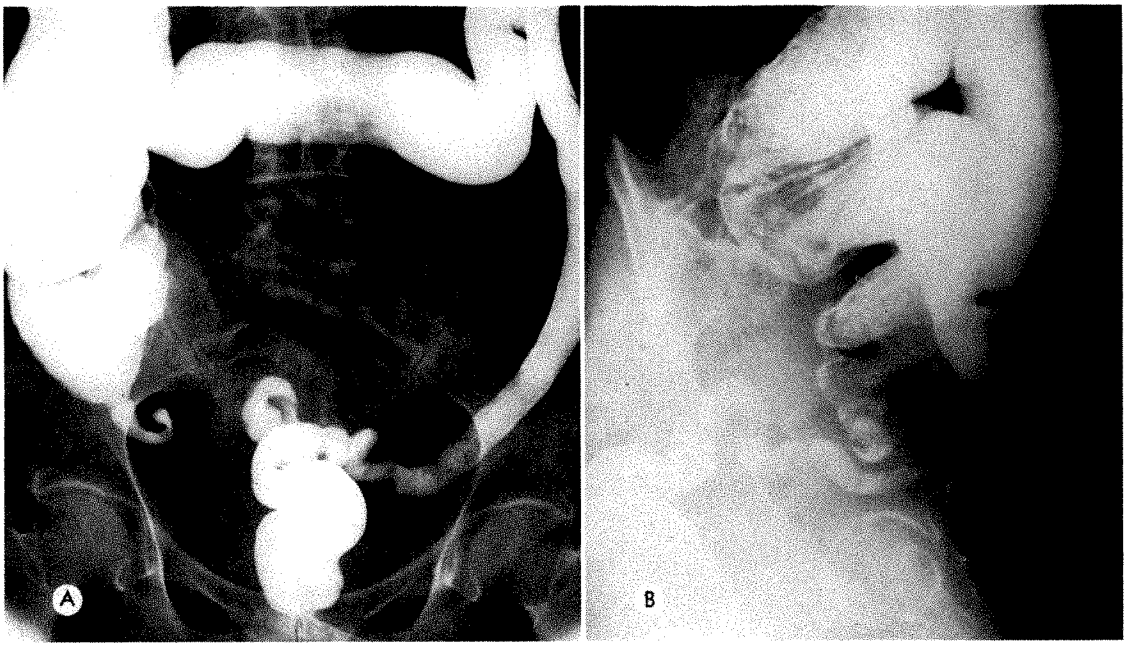


Fig. 3. Case II. (*A*) Anteroposterior and (*B*) lateral barium enema studies showing a normal appearing colon except for some loss of haustrations. The fistulas are not demonstrated.

sues and numerous adhesions. The small intestine was inadvertently opened in one place and in many areas the muscularis of the intestine was stripped away during blunt dissection.

The opening in the small intestine was closed in the usual manner, using gastrointestinal chromic and fine silk suture, but it was impossible to peritonealize any of the areas of intestine denuded of muscularis. The patient made a slow but progressive recovery and was discharged 10 days after surgery.

About 1 week after discharge, she noted fecal material draining from the vagina and was readmitted. A barium enema study was ordered and demonstrated a fistulous communication between the sigmoid and vagina (Fig. 1, *A* and *B*). A transverse colostomy was performed on May 4, 1961; however, fecal material continued to drain from the vagina. Re-examination on May 10, 1961, utilizing the vaginal technique described, revealed the original rectovaginal fistula as well as 2 other fistulas between the vagina and the terminal ileum (Fig. 2, *A* and *B*). The patient was returned to surgery and the 2 ileal fistulas were resected. The rectovaginal fistula was repaired and there was prompt cessation of the vaginal discharge. On July 19, 1961 the colostomy was closed and since then the patient has had no further difficulties.

Comment. A barium enema study was ordered in expectation of demonstrating the fistulous communication with the vagina. When a rectovaginal fistula was visualized, it was assumed that this was the entire source of the vaginal discharge. This false conclusion based on incomplete information led to the surgical failure of the colostomy. The direct vaginal approach was subsequently performed and the occult fistulas were demonstrated.

Case II. E.M., a 59 year old white female, was admitted to the hospital on December 25,

---

←

Fig. 2. Case I. (*A*) Spot vaginogram. Three fistulous tracts are now demonstrated: 2 to the ileum, not visualized on the barium enema study, and 1 to the sigmoid as noted in Figure 1*B*. (*B*) Conventional roentgenogram made in the anteroposterior position. Detail of the fistulous tracts is sacrificed, but the barium can be seen to traverse the terminal ileum to the cecum. There is also barium in one loop of the sigmoid. The tubing seen in the center of the roentgenogram leads to a suprapubic cystotomy.

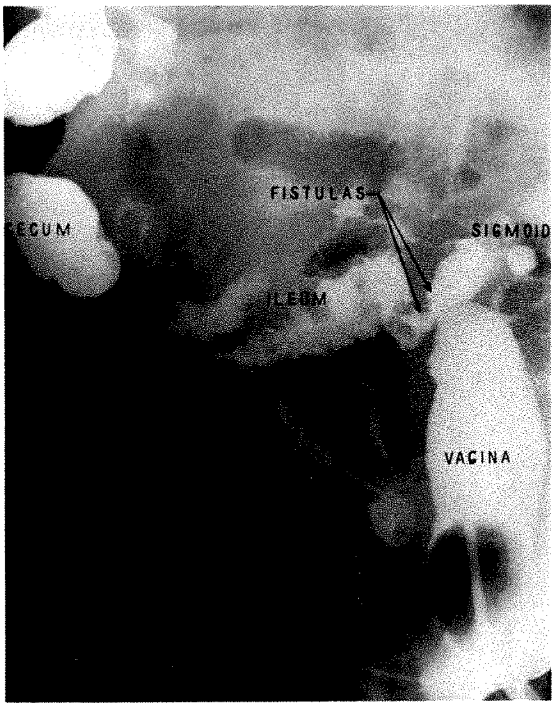


Fig. 4. Case II. Vaginogram demonstrating fistulas from the sigmoid and ileum to the vagina. These were not demonstrated by the conventional barium enema study (Fig. 3).

1961 with profuse vaginal fecal drainage of 3 weeks' duration. One and one-half years prior to admission the patient underwent a total hysterectomy and bilateral salpingo-oophorectomy for a papillary adenocarcinoma of the right ovary. This was followed by cobalt teletherapy delivering a tumor dose of 4,500 r over a 5 week period.

A barium enema study was requested and performed but failed to reveal any fistulous tracts (Fig. 3, *A* and *B*). This was followed on the same day by vaginography which disclosed a fistula with the sigmoid as well as a second fistula with the terminal ileum (Fig. 4). At surgery the terminal ileum and rectosigmoid were found to be encased in a mass of recurrent tumor adherent to the vagina. The mass was removed along with a portion of the sigmoid and terminal ileum. The small intestine as well as the large intestine was reapproximated and a transverse colostomy performed. Immediately following the operation the vaginal discharge ceased and the patient's general condition gradually improved. She was discharged in good condition.

Comment. The usual barium enema study failed to show the source of the vaginal discharge. This was followed immediately by vaginography which revealed both fistulas and led to the correct surgical approach.

CONCLUSIONS

Vaginal fistulous communications with the colon and rectum may or may not be demonstrated by a barium enema examination. Quite often more than one fistula is present and some of these may communicate with the small intestine. Vaginal fistulous communications with the small intestine cannot be demonstrated by a barium enema study. It is imperative that detailed information be obtained so as to avoid erroneous conclusions that might lead to surgical failure. We believe that vaginography is a more direct and reliable method for the demonstration and localization of vaginal fistulas and pitfalls inherent in the conventional barium enema study are avoided. If more than one fistulous tract is present, all will be demonstrated by this technique. Communications with the small bowel are easily shown and with this more complete information the surgeon is able to make the proper decision as to the type of corrective surgery needed.

In addition to the 2 reported cases, we have examined other patients with vaginal fistulas using the vaginographic technique rather than the barium enema study. In every case, we have been able to demonstrate accurately all fistulous tracts and these have been confirmed at surgery. We have observed no untoward effects from the use of barium sulfate in this procedure and feel that it is an excellent contrast medium for demonstration of fistulous tracts providing a thin solution is employed.

David S. Dann, M.D.
The Menorah Medical Center
4949 Rockhill Road
Kansas City 10, Missouri

REFERENCE

1. Frich, H. C., II. Study of complications in surgical and radiation therapy of cancer of cervix. *Surg., Gynec., & Obst.*, 1960, *111*, 493-506.

VAGINOGRAPHY*

By FRED O. COE, M.D.
WASHINGTON, D. C.

ON SEVERAL occasions during the past few years the author has been requested to demonstrate roentgenographically certain pathologic conditions involving the vagina.

Some of the conditions in which vaginography is of value are as follows: fistula between the vagina and some portion of the large or small intestine or appendage thereof, vesicovaginal fistula or a fistula between the vagina and any other organ, and abnormalities of the vagina either congenital or acquired. A careful review of the literature disclosed only 2 articles in which vaginograms were mentioned: one by Dante and his co-workers,[1] who used a Foley catheter in the vagina for hysterosalpingography and colpohysterosalpingography, and the other by Katzner and Trachtman,[2] who reported a case in which the vagina of a 7 year old girl was distended with 40 per cent hippuran solution to demonstrate an ectopic ureter, the patient being placed in the Trendelenburg position. Neither of these methods are the same as the technique to be reported.

METHOD

The bulb on the Bardex tube is inflated to about 6 cm. in diameter and the stem is clamped. The stem for administration of the barium enema is also clamped. The labia are separated and the tip of the Bardex tube is inserted. The patient holds the bulb firmly against the introitus. A large gauge hypodermic needle is introduced into the stem for the central channel of the Bardex tube and at least 25 cc. of any of the radiopaque materials used for intravenous administration is injected. Only contrast media that can be used for intravenous injection should be employed as escape may take place into either the peritoneal cavity or, as in one instance, into the venous system. If the inflated bulb is held firmly against the introitus, there should be no leakage. After the injection anteroposterior stereoscopic roentgenograms or, better yet, anteroposterior stereoscopic and both oblique roentgenograms are obtained. The process is absolutely painless and without danger and in some cases gives valuable diagnostic information.

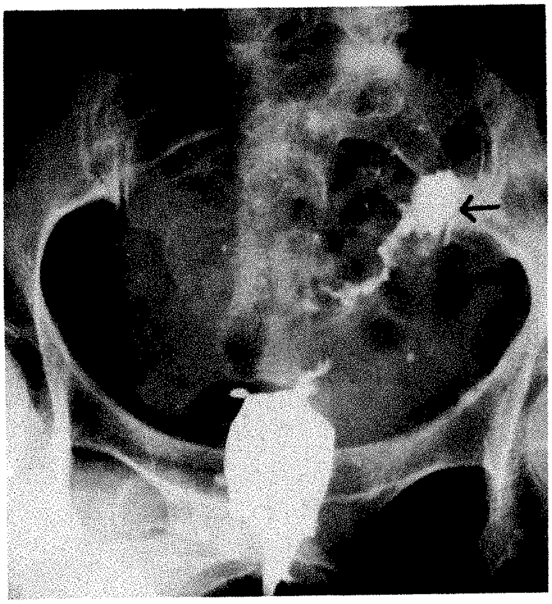


Fig. 1. Case II. Vaginogram showing fistula extending from posterior portion of vagina laterally on left side for 10 cm., entering sigmoid and a small fistula on the right.

ILLUSTRATIVE CASES

Case I. The patient was a nulliparous female, 26 years of age, complaining of some vaginal discharge. On vaginal examination there appeared to be a pouch extending backward from the dorsal wall of the vagina. A vaginogram showed an anomalous development of the vagina but a normal anterior vaginal cavity with a normal cervix protruding into the opaque shadow. Posteriorly just within the introitus was a blind pouch about 30 mm. long and 15

---

* From the Radiological Clinics of Drs. Groover, Christie & Merritt. Radiologist to Doctors Hospital, Washington Hospital Center and Sibley Hospital, Washington, D. C.

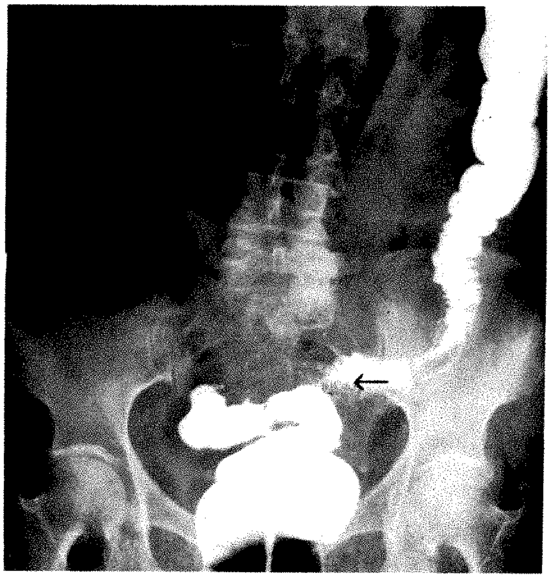


Fig. 2. Case II. Barium enema study following vaginography shows fistulous tract entering sigmoid.

mm. wide, ending in a smoothly rounded cul-de-sac. There was no escape of the opaque material into the surrounding tissues. This case represents an anomalous development of the vagina in which there was a blind pouch extending backward toward the rectum.

Case II. The patient was a 69 year old female who had had a total hysterectomy 10 years previously for a carcinoma of the uterus. Following operation radiation therapy was instituted to the pelvis. The previous year the patient developed a mass in the pelvis, which was suspected of being a recurrence of the carcinoma. At operation a granuloma resulting from a rupture of a diverticulum was found low in the pelvis. The patient made a good recovery except for the fact that she passed some gas and, at times, a small amount of feces through the vagina. On repeated physical examinations no true fistulous tract could be found. A vaginogram was made and showed a fistula extending from the posterior portion of the vagina laterally on the left side for a distance of about 10 cm. (Fig. 1). There was a second small fistulous tract extending about 15 mm. from the right posterior margin of the vagina but ending in a blind sac. After the vaginography, a barium enema study was performed (Fig. 2) and a fistulous tract from the vagina to the irregular portion of the sigmoid was clearly shown. The patient was operated on soon after this and the findings were confirmed.

SUMMARY

1. Some indications for vaginography have been cited.

2. A simple, safe and adequate method is described.

3. The method is of real value in selected cases.

1835 Eye Street, NW
Washington 6, D. C.

REFERENCES

1. Dante, C., Gluck, J. C., and Calandra, N. Hysterosalpingography and colpohysterosalpingography; new technics and modifications. *Obst. & Gynec.*, 1959, *13*, 563–567.
2. Katzner, P., and Trachtman, B. Diagnosis of vaginal ectopic ureter by vaginogram. *J. Urol.*, 1954, *72*, 808–811.

CELIOGRAPHY WITH IOTHALAMIC ACID*

EXPERIMENTAL STUDIES IN DOGS AND RATS

By ALEXANDER R. MARGULIS, M.D.,† GALEN B. COOK, M.D.,‡ GEORGE L. TUCKER, M.D.,‡ *and* SIDNEY L. SALTZSTEIN, M.D.§

CONVENTIONAL roentgenographic studies of the gastrointestinal tract with contrast material depend on opacification of its lumen. Only the intraluminal protrusions of the diseased wall are outlined. Displacements of the entire structure also are observed. A very important consideration for the surgeon, however, is the extension of the tumor or disease process outside the gastrointestinal wall. Also, visualization of the hepatic outline preoperatively would add important information.

Water soluble, iodine containing contrast media introduced into the peritoneal cavity are quickly absorbed and disappear before satisfactory roentgenograms in various projections can be obtained. Coating of the external surfaces is poor. Presently available water soluble media are irritating and painful.[1,2] Particulate contrast media placed in the peritoneal cavity produce fibrosis and adhesions. The ideal material would be slightly soluble so that absorption is prolonged but occurs before adhesions develop. Such a material would coat the surface of the intraperitoneal organs, then be absorbed and excreted by the kidney. The rate of disappearance from the peritoneal cavity should permit adequate roentgenograms to be taken. The material should be nontoxic, nonirritating, and painless.

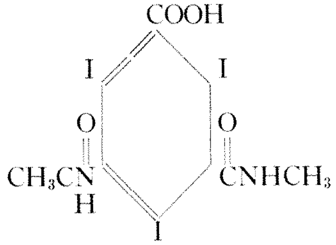
In this report our experiences with the use of iothalamic acid* in the peritoneal cavity of dogs and rats is presented.

MATERIAL

Iothalamic acid is a white powder of low solubility. Its sodium salt is commercially known as angio-conray and its methylglucamine salt as conray.* Both salts are extremely soluble.

Iothalamic Acid

(5-acetamido-2,4,6-triiodo-N-methylisophthalamic acid)



Molecular weight 614

Iodine content 62%

The acid has a pH of 1 in 50 per cent suspension and 1.7 in 35 per cent suspension. The LD_{50} in mice intraperitoneally is 18,192 mg. per kg., as compared to that of conray of 17,000 mg. per kg. intravenously. In albino rats, weighing 350 gm., to which 2 ml. of 35 per cent suspension of iothalamic acid was administered intraperitoneally, the peritoneal aspirate had a pH

---

* Mallinckrodt Pharmaceuticals, Mallinckrodt Chemical Works, St. Louis, Missouri.

* From the Edward Mallinckrodt Institute of Radiology,† and the Departments of Surgery‡ and Pathology,§ Washington University School of Medicine, St. Louis, Missouri.

This work was supported by a grant-in-aid from Mallinckrodt Pharmaceuticals, Mallinckrodt Chemical Works, St. Louis, Missouri.

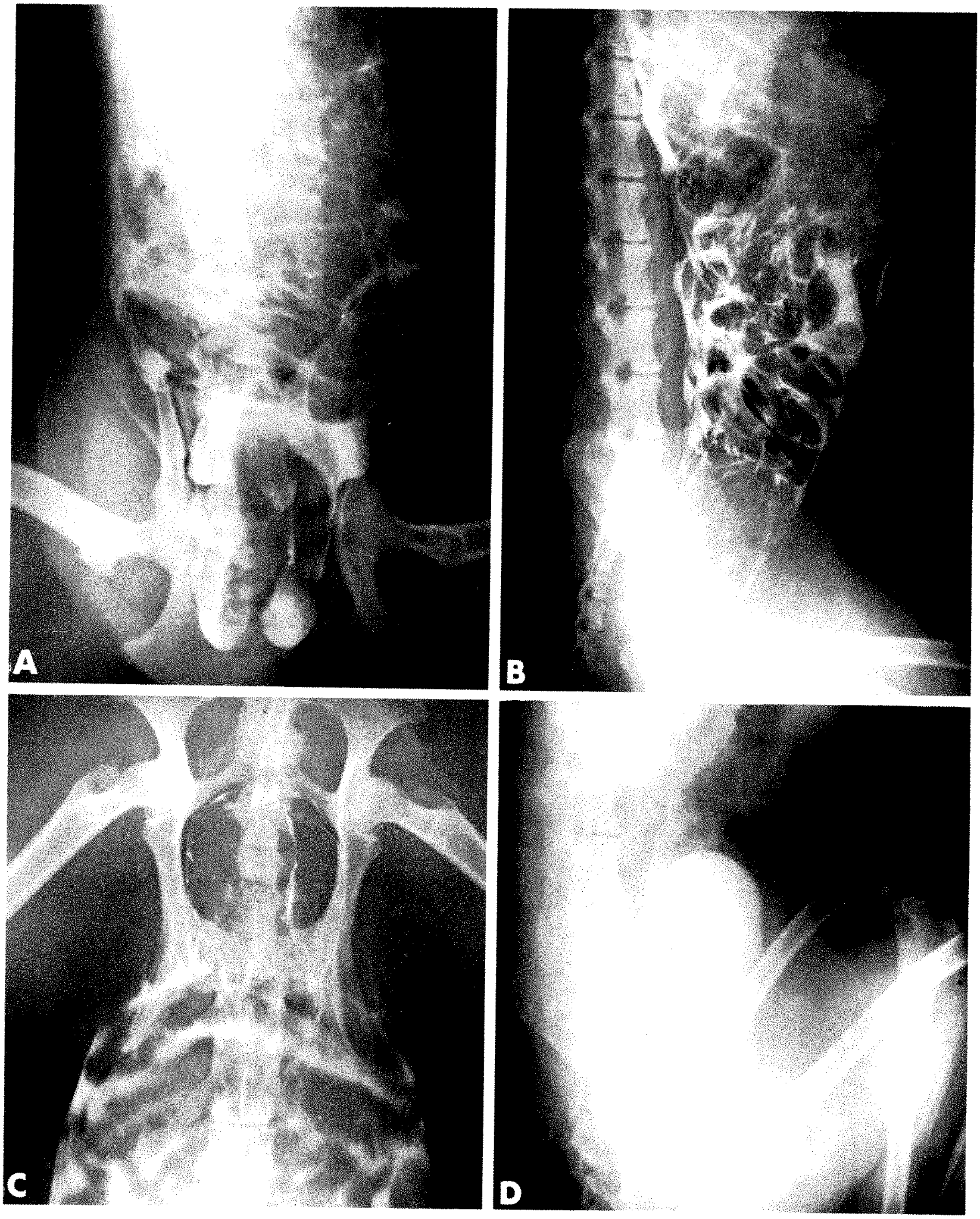


FIG. 1. Inframesocolic injection of iothalamic acid into the peritoneal cavity in dog. (*A*) Anteroposterior roentgenogram in upright position. The contrast medium is outlining the bowel, urinary bladder and cul-de-sac. (*B*) In lateral projection, these same structures can be well seen. (*C*) In the Trendelenburg position, the bladder and pelvic organs are outlined. (*D*) One hour following administration, the peritoneal cavity is clear and the material is seen in the urinary bladder.

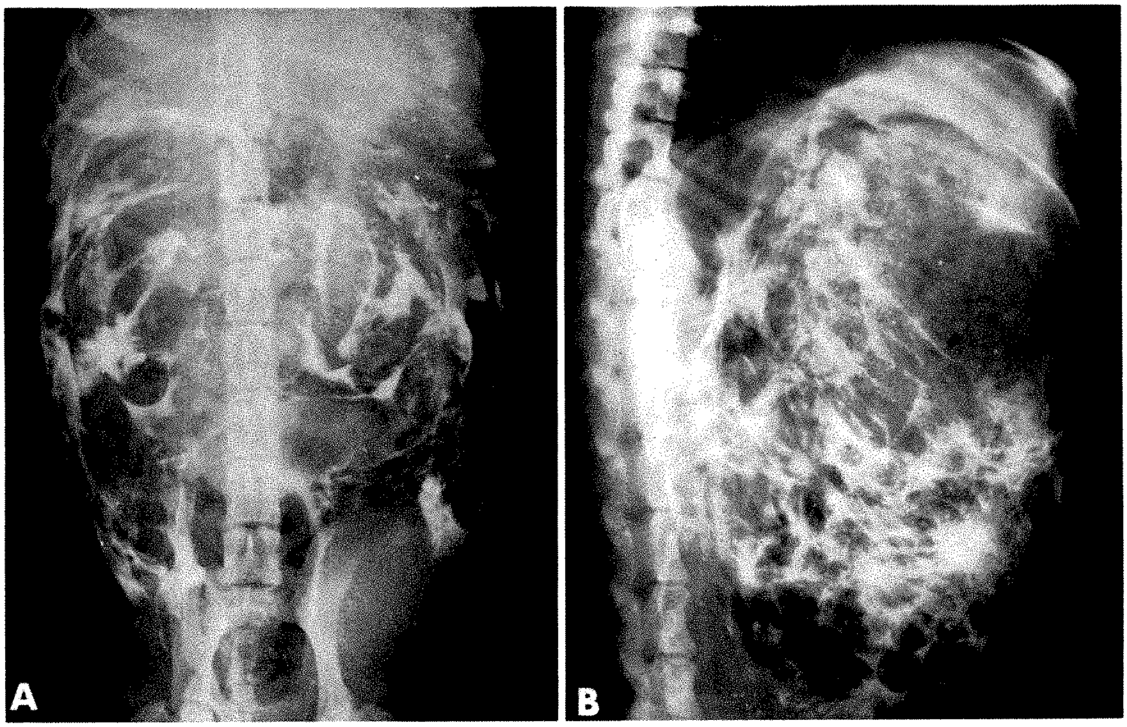


FIG. 2. Supramesocolic injection of iothalamic acid into the peritoneal cavity. (*A*) The liver is outlined, the left and right lobes can be seen. The bowel loops are separated and their outline is well seen. The stomach and duodenum are outlined. (*B*) Same dog, lateral projection. The outline of the liver, stomach, and bowel is again well shown.

of 3.5 immediately after injection and a pH of 3.8 thirty minutes after injection.

PROCEDURE

In dogs weighing over 15 kg., local procaine anesthesia was administered and a bardic† intravenous catheter placement unit, No. 14, with an 8 inch catheter was introduced into the peritoneal cavity. The catheter was threaded through the needle and the needle withdrawn. The catheter was placed either above or below the transverse mesocolon. Its position was localized by roentgenography, then 15 to 30 ml. of 35 per cent iothalamic acid followed by 100 to 200 ml. of air were introduced into the peritoneal cavity and the catheter was removed. Frontal and lateral roentgenograms were obtained in recumbent, upright, and Trendelenburg positions. The dogs did not appear to suffer any pain.

In anesthetized rats, 4 ml. of the 35 per cent suspension followed by 5 to 10 ml. of air were injected into the peritoneal cavity via a No. 20 gauge needle. In some of the rats, small radiolucent foreign bodies with identifying metallic markers were placed in the peritoneal cavity before the injection. Roentgenograms were then obtained as in dogs. In animals of both species, 1 hour follow-up roentgenograms were also obtained.

To test for local toxicity, 6 rats and 6 dogs had iothalamic acid injections in the above manner, and 2 of each species had laparotomies at 1 hour, 18 hours, and 2 weeks after injections. Biopsies of liver, kidney, and small bowel were also obtained. All were carefully examined for evidence of adhesions, inflammation or necrosis.

Other animals which had been subjected to this procedure 3 to 5 times were also carefully examined at laparotomy.

RESULTS

Roentgenograms of dogs and rats showed iothalamic acid to be a satisfactory medium

---

† C. R. Bard, Inc., Murray Hill, New Jersey.

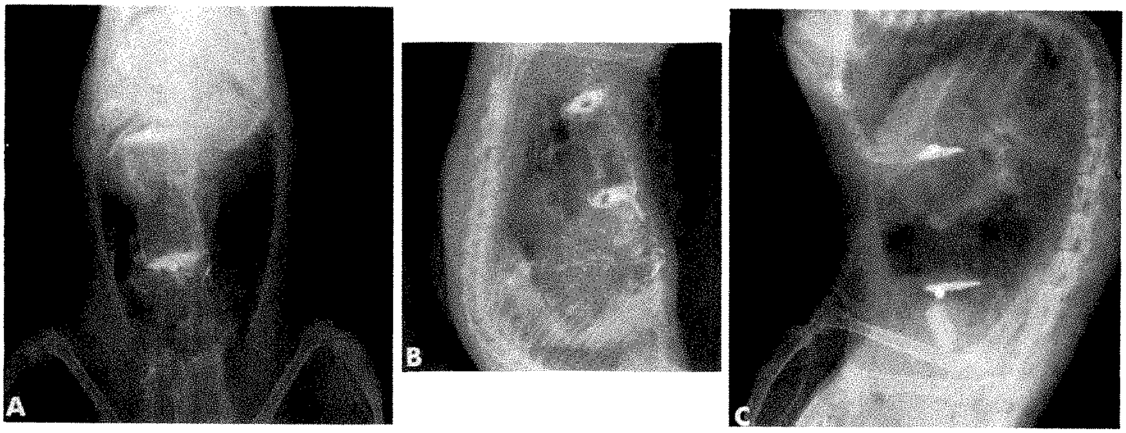


Fig. 3. A wooden foreign body was placed into the peritoneal cavity of a rat and iothalamic acid and air were introduced. Two metallic beads were fixed on two flat surfaces of the foreign body by Scotch tape. The liver, peritoneal organs, parietal-peritoneal surface and the foreign body are well outlined. (*A*) Anteroposterior projection. (*B*) Trendelenburg lateral projection. (*C*) One hour following administration of the material it has disappeared from the peritoneal cavity. Only the material caught between Scotch tape and the foreign body is visible.

for the outline of intraperitoneal organs (Fig. 1 through 3, inclusive). In 1 hour the material disappears from the peritoneal cavity and is excreted by the kidneys. The bladder is usually radiopaque on the 1 hour film.

The laparotomies on the 6 dogs and 6 rats used for the local toxicity tests showed no abnormalities and biopsies of liver, kidney, and small bowel were also normal. Similar studies of a dog that had 5 examinations with iothalamic acid 35 per cent also showed no abnormalities 1 week after the last celiography. One dog, used in preliminary studies, succumbed to general anesthesia. Autopsy showed no evidence of peritoneal or other toxicity.

Segments of dog ileum exposed for 20 minutes to hypaque powder, iothalamic acid powder, and a control segment were biopsied. No abnormalities were observed in the control loop or the loop exposed to iothalamic acid. The segment exposed to hypaque powder showed a small amount of subserosal edema.

Using the needle and catheter, the intestine of the dog was not punctured in any of the tests. In rats, using the sharp No. 20 gauge needle, occasionally the colon was punctured and the material introduced into it. These rats did not suffer from any complications.

DISCUSSION

These preliminary studies indicate that iothalamic acid may be a satisfactory medium for celiography. Its acidity does not appear to be a serious drawback. The 35 per cent suspension is satisfactory for spread through the peritoneal cavity. Air in conjunction with the liquid suspension has been helpful in upright and Trendelenburg positions for outlining the intraperitoneal organs. A search for other media that may be as nontoxic as iothalamic acid but of a pH closer to 7 is continuing.

SUMMARY

Experiences with iothalamic acid celiography and pneumoperitoneum in dogs and rats are presented.

Alexander R. Margulis, M.D.
Department of Radiology
University of California
San Francisco Medical Center
San Francisco 22, California

REFERENCES

1. Betoulieres, P., Jaumes, F., Voisin, G., and Gilbert, J. Supramesocolic opaque peritoneography. *J. de radiol., d'électrol. et de méd. nucléaire*, 1961, *42*, 611–615.
2. Birzle, H. Is peritoneography possible and useful as roentgenological method of examination? *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d Nuclearmedizin*, 1961, *95*, 824–829.

THE ROENTGEN MANIFESTATIONS OF MESENTERIC ADENITIS*

By M. H. POPPEL, M.D.
NEW YORK, NEW YORK

MESENTERIC adenitis, lymphadenitis or lymphadenopathy may be specific or nonspecific.

The specific variety occurs in some general diseases such as tuberculosis, typhoid or syphilis, and in some neoplastic diseases such as carcinoma or lymphoma. Most of the calcifications seen in the specific variety are the result of tuberculosis.

The nonspecific variety is the subject of this paper. It is a recognized clinical entity of unknown etiology. It often precedes or follows an upper respiratory infection. It is more common in females and occurs most often between the ages of 5 to 15 years, although it may be seen at any age. Allergy, parasites and viruses have been etiologically mentioned.

CLINICAL MANIFESTATIONS

The clinical manifestations often resemble acute appendicitis and accordingly may lead to a laparotomy.

The onset is usually acute with a dull aching pain in the right lower quadrant. Occasionally, the pain may be colicky and referred to the umbilical region. There is right lower quadrant tenderness which may

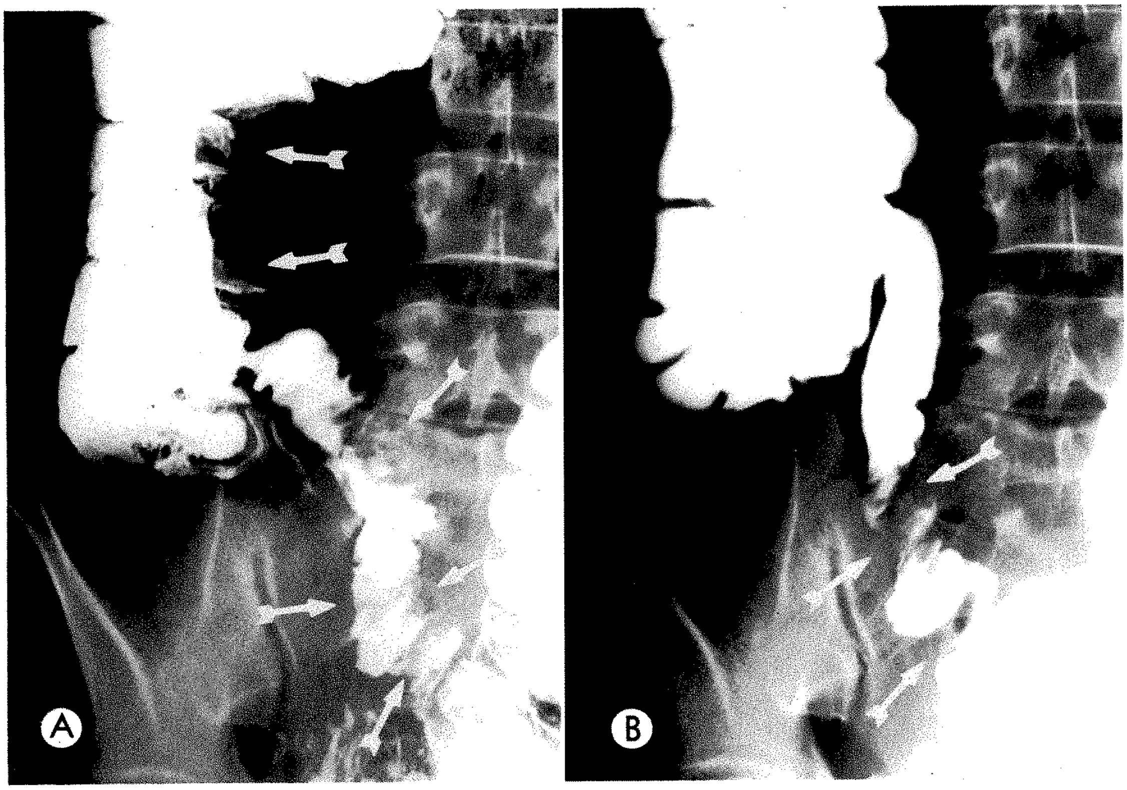


Fig. 1. (*A*) Indentures on the terminal ileum and a large scalloped indenture on the medial border of the ascending colon due to enlarged lymph nodes. The ileal folds are enlarged, probably due to edema. (*B*) Indentures on the terminal ileum. This study was part of the same examination as *A*. Note variability.

---

* From the Department of Radiology of the New York University Medical Center.

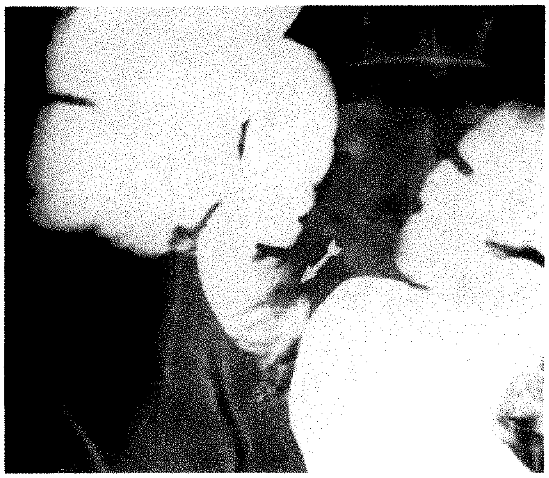


Fig. 2. Indentures on the terminal ileum.

extend upward towards the left along the course of the root of the mesentery. There may be muscular rigidity, nausea and vomiting.

There is a low grade temperature of 99–100° F. with a slight to moderate leukocytosis with a near normal differential count.

There may be recurrent attacks.

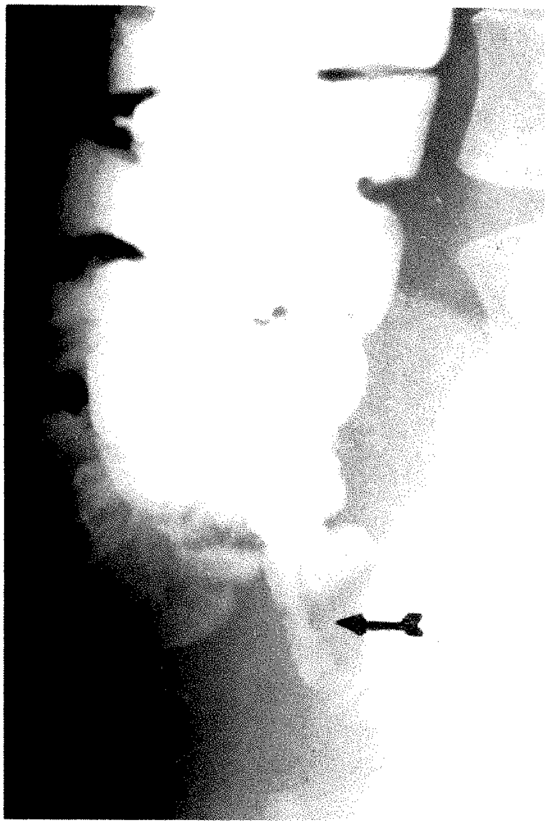


Fig. 3. Indentures on the terminal ileum.

ANATOMY

The mesenteric lymph nodes lie between the layers of the mesentery where they form three main groups: A series of juxtaintestinal lymph nodes which lie close to the walls of the small bowel and accordingly are of extreme importance to the roentgenologist because of their possible detection when enlarged; an intermediate series which lie in relation to the branches of the superior mesenteric artery; and a group of large lymph nodes around the stem of the superior mesenteric artery.

A more local right lower quadrant classification consists of:

1. The ileal lymph nodes which lie in the lowest part of the mesentery.
2. An appendicular lymph node which is sometimes seen in the mesentery of the appendix.
3. The anterior ileocolic lymph nodes

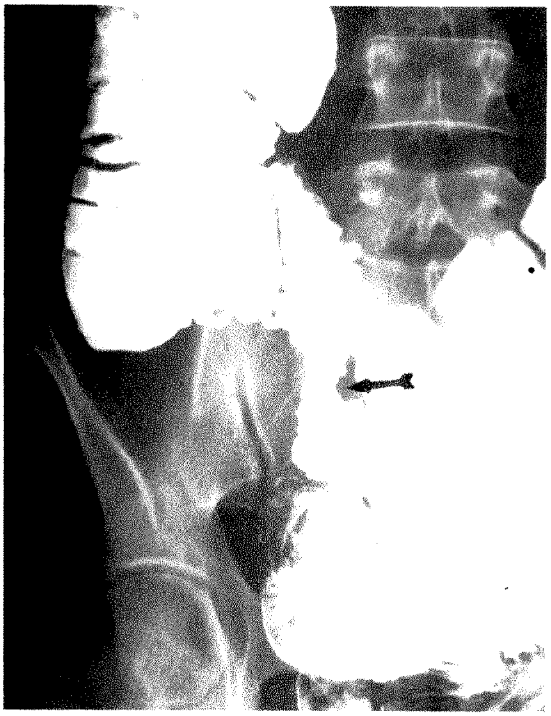


Fig. 4. Indentures on the terminal ileum.

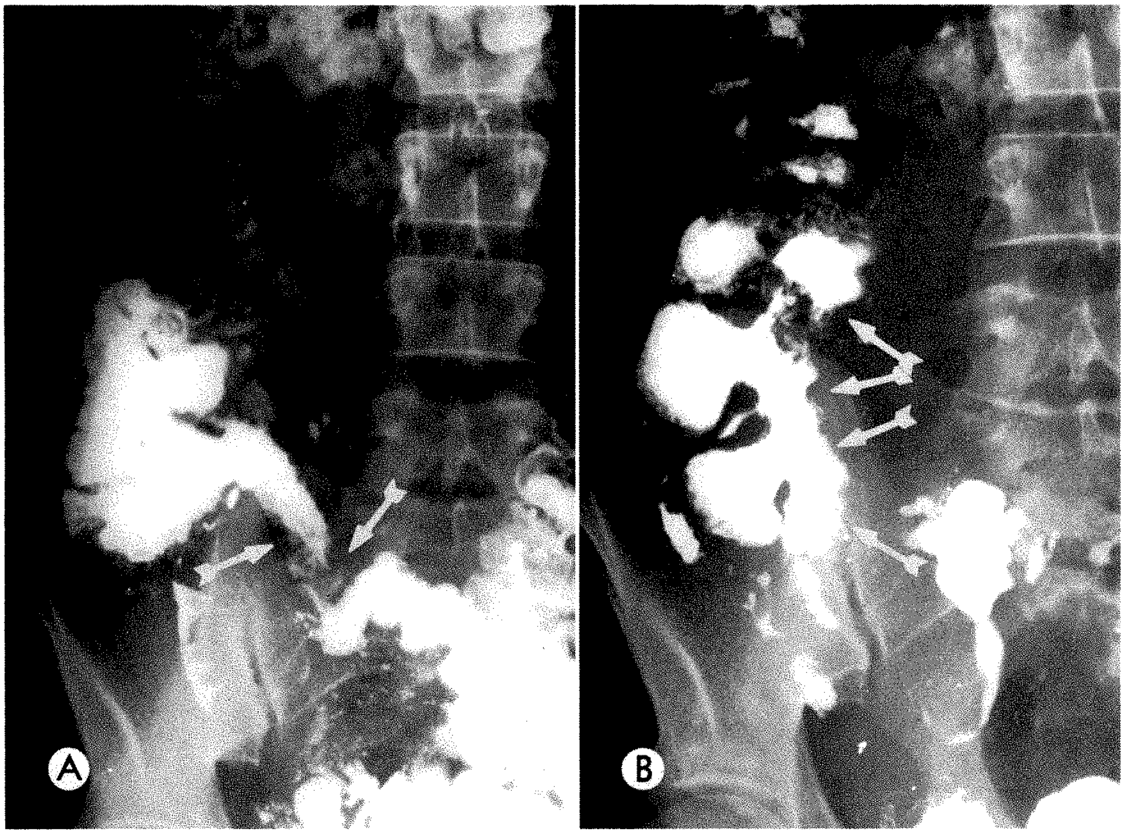


Fig. 5. (*A*) Indentures on the terminal ileum and (*B*) on the medial border of the ascending colon.

which lie in the anterior ileocolic fold of the peritoneum.

4. The posterior ileocolic lymph nodes which lie in the angle between the ileum and the cecum and in the angle between the ileum and the ascending colon.
5. The epicolic lymph nodes which are small and lie in the appendices epiploicae and thus in close relation to the wall of the bowel.
6. The paracolic lymph nodes which lie along the medial border of the ascending colon.

PATHOLOGIC CHANGES

Grossly, there is inflammatory enlargement, mainly of the mesenteric lymph nodes in the ileocecal angle, which results from marked hyperplasia of the lymphoid and reticulo-endothelial tissue. The microscopic picture varies with the severity of the inflammation. If extreme, the sinuses will be crowded with polymorphonuclear cells and patches of necrosis will be scattered throughout the lymph nodes which will go on to abscess formation. This suppurative form, however, is not common.

ROENTGEN MANIFESTATIONS

Because of the similarity to acute appendicitis, barium examination is withheld so that only an occasional patient is subjected to a small bowel roentgen study.

One or more small or large indentures on the lower segment of the ileum or on the medial border of the ascending colon, most often near the ileocecal valve, may be demonstrated. The appearance varies considerably from study to study, even on any one examination (Fig. 1 through 5, inclusive), because of the extrinsic origin and the associated spasm, irritability and intolerance of the bowel. The indentures usually result from enlarged mesenteric lymph

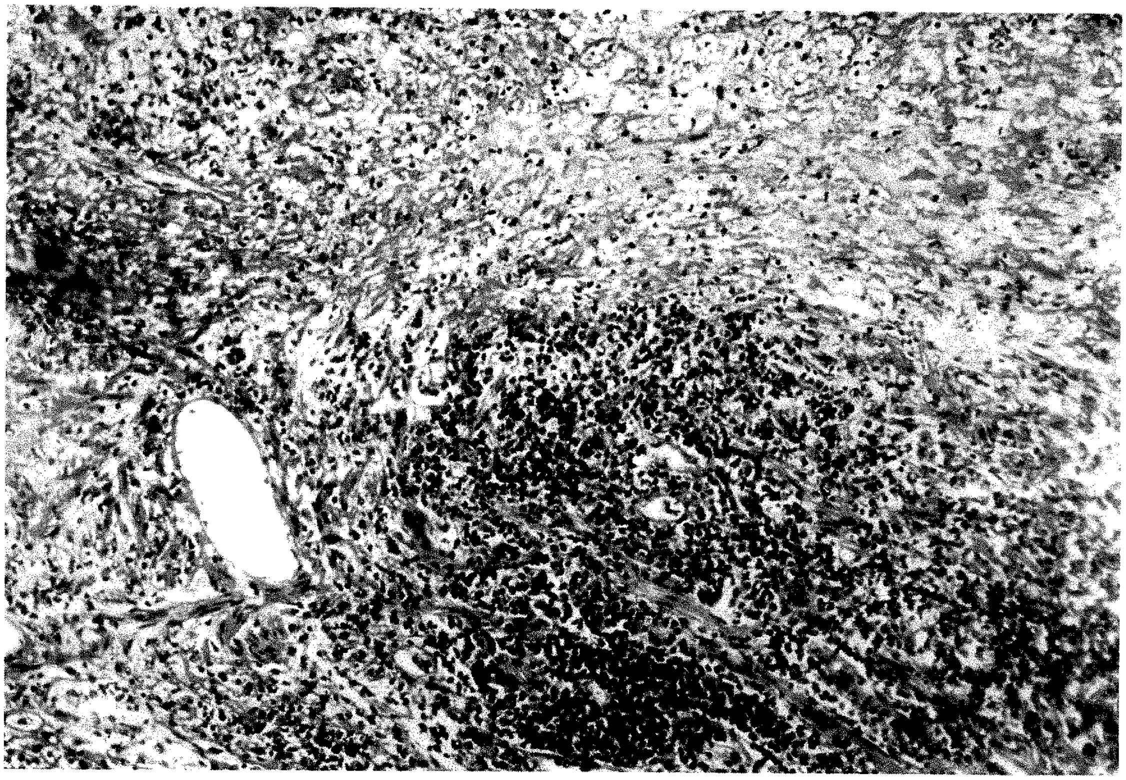


Fig. 6. Microphotograph of a section of the lymph node removed from the mesentery indicating mesenteric adenitis.

nodes (and occasionally, as in our case, additionally from the paracolic lymph nodes) and may, depending on size, increase the space between two or more coadjacent loops or possibly obstruct if sufficiently enlarged. The bowel itself may be displaced if the lymph nodes mat up and preempt any significant amount of space.

The ileum and ascending colon are free of any structural abnormalities. The mucosa (including the ileocecal valve region) is intact but may appear enlarged if involved by local edema.

There is hyperperistaltic activity.

The above changes may become complicated if suppuration of the lymph nodes develops at which time structural bowel changes with or without fistulae will occur.

Fluoroscopically, there is diffuse tenderness in the right lower quadrant.

REPORT OF A CASE

A 32 year old white female was admitted with a history of right lower quadrant pain and diarrhea for the past month. The patient had been admitted 6 months previously for recurrent diarrhea and anemia and was discharged with a diagnosis of hypoproteinemia.

At surgery (13 days after the roentgen examination), the mesentery of the small bowel was found to be swollen and edematous with large mesenteric lymph nodes, 1 to 4 cm. in size. There was no structural abnormality of the small bowel nor of the colon. A 1.5 cm. sized lymph node was removed for study (Fig. 6). Microscopic examination revealed extensive necrosis resulting in distortion and destruction of the normal architecture. In the necrotic areas there were many nuclear fragments and a meshwork of pink-staining fibrin. Scattered islands of lymphocytes were present. The diagnosis was necrosis of a mesenteric lymph node.

Microbiology. Cultures showed a moderate number of *Staphylococcus albus* colonies and chains of gram positive cocci identified as nonhemolytic streptococci. The culture for acid fast bacilli was negative. L.E. cells and phenomenon tests were negative.

SUMMARY

Nonspecific mesenteric adenitis is a clinical entity of unknown etiology although allergy, parasites and viruses have been mentioned as possible causes. The findings are briefly discussed and a report of a case is presented.

550 First Avenue
New York 16, New York

REFERENCES

1. Boyd, W. A Textbook of Pathology; An Introduction to Medicine. Seventh edition. Lea & Febiger, Philadelphia, 1961, pp. 1106–1107.
2. Ochsner, A. Diseases of intestines. In: A Textbook of Medicine. Tenth edition. Edited by Cecil, R. L., and Loeb, R. F. W. B. Saunders Company, Philadelphia, 1959, p. 839.
3. Wilensky, A. O., and Hahn, L. J. Mesenteric lymphadenitis. *Ann. Surg.*, 1926, *83*, 815–826.

INTRAMURAL HEMATOMA OF THE JEJUNUM*

A CASE REPORT

By GORDON J. CULVER, M.D., *and* HERBERT S. PIRSON, M.D.
BUFFALO, NEW YORK

PREVIOUSLY we reported an intramural hematoma of the jejunum[2] as a complication of anticoagulant therapy. At this time, we are reporting a case which was the result of trauma, a rare cause of hematoma in the jejunum. In both of these instances and a case of intramural hematoma in the duodenum,[1] we have been able to make the diagnosis by the characteristic roentgenographic appearance.

REPORT OF A CASE

J.I., a 16 year old white male, while driving a golf cart, hit a tree. In the accident, the umbilical region of his abdomen struck the steering mechanism. After the accident, the patient experienced some soreness, but was relatively free of any major pain. On the following day, he gradually began to have severe abdominal pain which caused him to double up.

He was admitted to the hospital and had

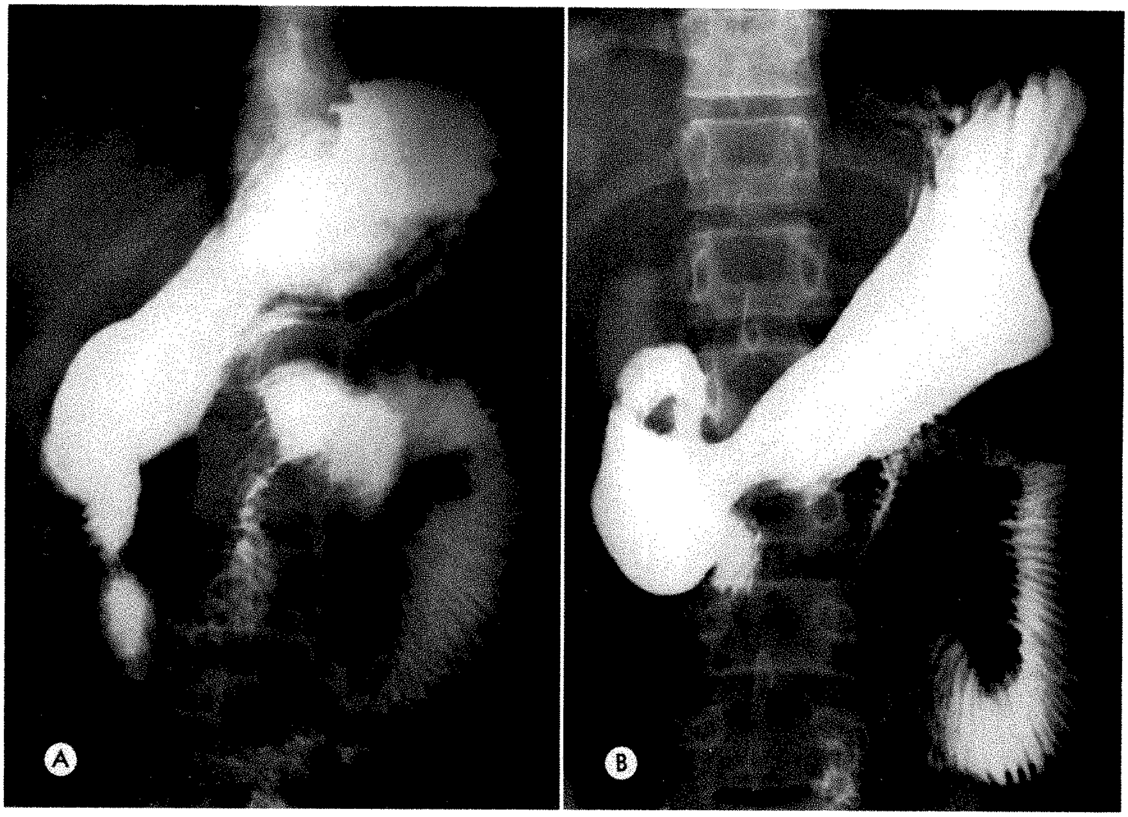


FIG. 1. (*A* and *B*) Upper gastrointestinal roentgenograms showing an intramural mass in the jejunum, starting at the ligament of Treitz and extending 10 to 12 inches, with stretching of the fold pattern and crowding together of the valvulae conniventes. This produces the coil spring appearance characteristic of an intramural hematoma.

---

* From the Department of Radiology of the State University of New York at Buffalo, and the Radiology Department of The Buffalo General Hospital, Buffalo, New York.

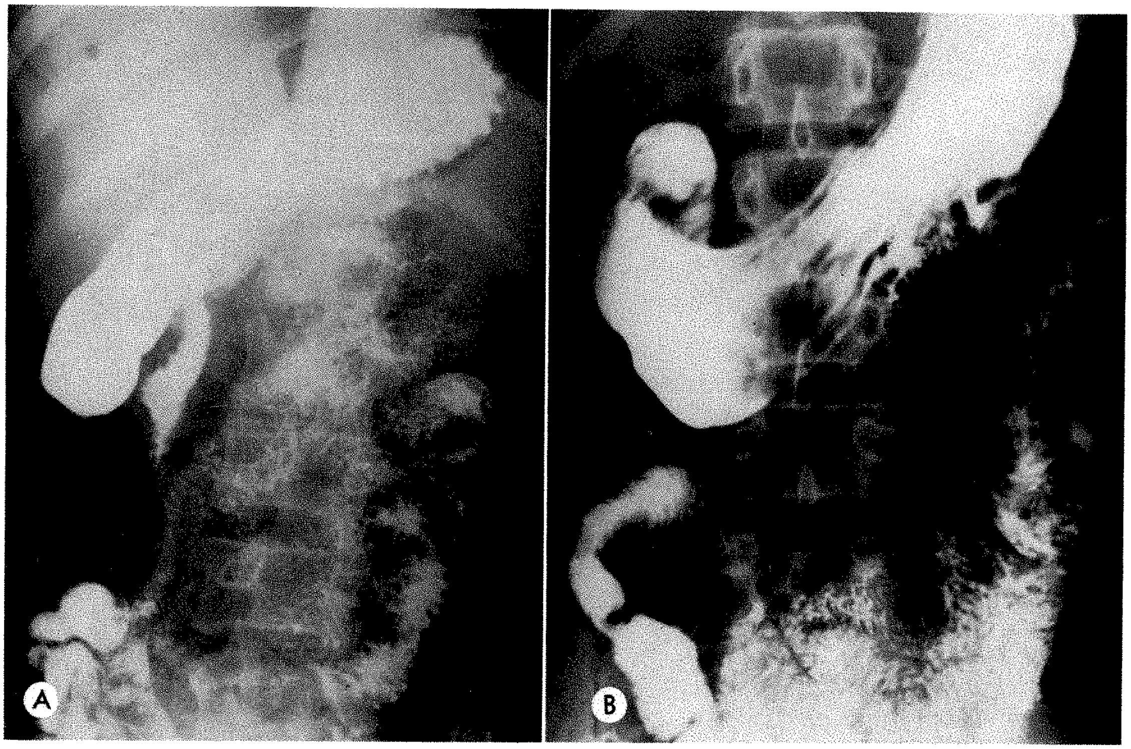


Fig. 2. (*A* and *B*) Upper gastrointestinal roentgenograms made 2 weeks later showing a normal jejunal pattern, indicating resorption of the hematoma.

several episodes of emesis. The abdominal pain gradually subsided over a 3 day period after which he had a recurrence lasting for one day. The laboratory work and physical examination were not remarkable except for a mild elevation of the white blood cell count.

Treatment consisted of a bland diet and Pro Banthine, Compozine and Miltown.

Roentgenograms of the abdomen were made on the second and third days following the trauma and were negative. Twelve days after the accident cholecystography and upper gastrointestinal series were performed. The cholecystogram was normal. The upper gastrointestinal series showed a normal stomach and duodenum. The jejunum, starting at the ligament of Treitz and extending 10 to 12 inches showed stretching of the fold patterns with increase in caliber associated with crowding together of the valvulae conniventes, typical of an intramural mass. This produced the coil spring effect of an intramural hematoma (Fig. 1, *A* and *B*).

The upper gastrointestinal study was repeated 2 weeks later and showed a completely normal jejunal pattern (Fig. 2, *A* and *B*). It was felt that the patient had an intramural hematoma which underwent resorption.

DISCUSSION

An intramural hematoma of the small bowel may be caused by trauma and increased bleeding tendencies such as Henoch's purpura or as a complication of anticoagulant therapy. Invasion of the small bowel by a neoplastic process also has been suggested as another possible cause. Some cases have been reported with unknown etiology and have been called spontaneous. In many of these cases of spontaneous hematomas, some trauma which was not recalled by the patient may have been present.

Davis and Thomas[3] reviewed the literature in 1961, and found 45 cases of intramural intestinal hematoma. Since that time about 5 more cases have been reported.[2,6,10] Slightly over one-half of these hematomas were in the duodenum. Intramural hematoma of the duodenum is more common than intramural hematoma of the jejunum since the fixed position of the duodenum and its relation to the vertebral column is more vulnerable to direct trauma.

The roentgen diagnosis of intramural hematoma of the jejunum is based on the findings first described by Felson and Levin[4] indicating an intramural hematoma of the duodenum. These consist of an intramural mass associated with crowding together of the valvulae conniventes, producing a coil spring appearance. In the presently reported case and in our previously reported cases,[1,2] we have been able to make the diagnosis on the basis of this characteristic appearance. The 2 previously reported cases were confirmed at surgery. Although surgery has not been performed in this case and pathologic proof is lacking, the roentgenographic appearance followed by normal studies appears to be proof that a correct diagnosis has been made.

SUMMARY

A case of an intramural hematoma of the jejunum which resulted from direct trauma is presented. The diagnosis was made by the characteristic roentgenographic findings.

Gordon J. Culver, M.D.
The Buffalo General Hospital
100 High Street
Buffalo 3, New York

REFERENCES

1. Culver, G. J., and Pirson, H. S. Intramural hematoma of duodenum: case report. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *82*, 1032–1035.
2. Culver, G. J., Pirson, H. S., Milch, E., Berman, L., and Abrantes, F. J. Intramural hematoma of jejunum; case report. *Radiology*, 1961, *76*, 785–789.
3. Davis, D. R., and Thomas, C. Y. Intramural hematoma of duodenum and jejunum: cause of high intestinal obstruction; report of three cases due to trauma. *Ann. Surg.*, 1961, *153*, 394–398.
4. Felson, B., and Levin, E. J. Intramural hematoma of duodenum: diagnostic roentgen sign. *Radiology*, 1954, *63*, 823–830.
5. Garfinkel, B., Waleson, M., and Furst, N. J. Hematoma of duodenum; report of surgically proved case. *Am. J. Surg.*, 1958, *95*, 484–486.
6. Mirov, A. G. Intramural hematoma of duodenum. *Surgery*, 1962, *51*, 434–436.
7. Oppenheimer, G. D. Acute obstruction of duodenum due to submucous haematoma. *Ann. Surg.*, 1933, *98*, 102–195.
8. Rowe, E. B., Baxter, M. R., and Rowe, C. W. Intramural hematoma of duodenum; report of case with unusual complication. *A.M.A. Arch. Surg.*, 1959, *78*, 560–564.
9. Spencer, R., Bateman, J. D., and Horn, P. L. Intramural hematoma of intestine; rare cause of intestinal obstruction; review of literature and report of case. *Surgery*, 1957, *41*, 794–804.
10. Wiot, J. F., Weinstein, A. S., and Felson, B. Duodenal hematoma induced by coumarin. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1961, *86*, 70–75.

PANCREATIC CYSTADENOMA WITH INTESTINAL HEMORRHAGE*

By H. ROSENBAUM, M.D., P. J. CONNOLLY, M.D., A. R. W. CLIMIE, M.D., *and*
W. S. REVENO, M.D.
DETROIT, MICHIGAN

IN MOST of the cases of pancreatic cystadenoma reported in the literature the tumor is described as a true neoplasm most commonly located in the tail or body of the pancreas. It tends to expand slowly causing some discomfort from pressure and occasional pain aggravated by bending or motion. When it becomes large enough, it may become palpable and cause widening of the duodenal loop if it is located in the head of the pancreas. That is the extent of its symptomatology.

The patient whose case we are reporting had no previous symptoms of a pancreatic lesion but his illness started with a severe intestinal hemorrhage.

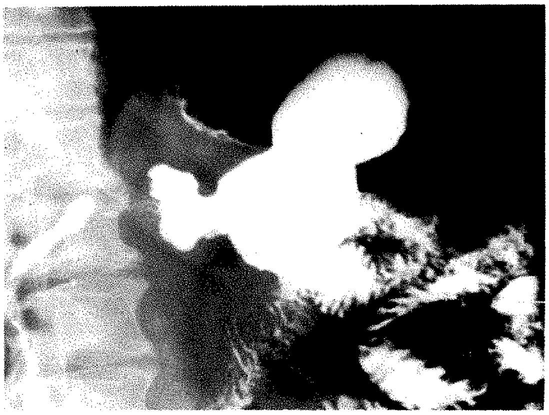


Fig. 1. Roentgenogram showing widening of duodenal loop with deformity of the duodenal wall.

REPORT OF A CASE

For 3 days before admission this 69 year old white male had had persistent diarrhea with passage of many tarry and bloody stools. He had very little pain and complained only of weakness, dizziness and some nausea. There was no history suggesting a cause for this attack. He appeared anxious, the skin was pale and cool, the blood pressure was 120/80 mm. Hg and the only significant finding was a poorly defined irregular mass in the right upper quadrant of the abdomen about 6 cm. below the costal margin. Hematocrit was 19 per cent, hemoglobin 6.1 gm. per 100 ml., red blood cell count 2.85×10^6/cu.mm. and the white blood cell count 11,500/cu.mm. A total of 9 units of whole blood was given during the first 3 days with a rise in hemoglobin to only 8.5 gm. per 100 ml. and hematocrit to 28 per cent.

Roentgen Findings. An esophagogram and upper gastrointestinal series on the third day showed no abnormality in the esophagus or stomach. There was a soft tissue mass superimposed upon the upper half of the right kidney and the lower margin of the liver with air surrounding it in the retroperitoneal space. The duodenal bulb appeared irregular and deformed. The principal abnormality was a widening and compression of the duodenal sweep (Fig. 1) giving the impression of a large retroperitoneal soft tissue mass in the region of the pancreatic head. The duodenal mucosal pattern was distorted and appeared to be invaded or involved by this tumor mass, conceivably of a malignant nature. Because of the air in the retroperitoneal space, the possibility of a perforated ulcer with abscess formation was considered; however, at no time was there any extravasation of barium into the retroperitoneal space. There was no intestinal obstruction and after 2 hours small bowel motility and mucosal pattern were thought to be within normal limits. Follow-up roentgenograms on the following day showed very little change. The possibility of an aortic aneurysm with rupture was also considered but there was no soft tissue calcification to support such a diagnosis.

Operative Findings. An operation was performed (P.J.C.) on the fifth day after 23 units of blood had been given. At this time the hematocrit was 29 per cent, hemoglobin 9.7 gm. per 100 ml. and the red blood cell count 3.00×10^6/cu.mm. On opening the abdomen, a huge tumor

---

* From the Departments of Medicine, Surgery and Pathology, Harper Hospital and Wayne State University College of Medicine.

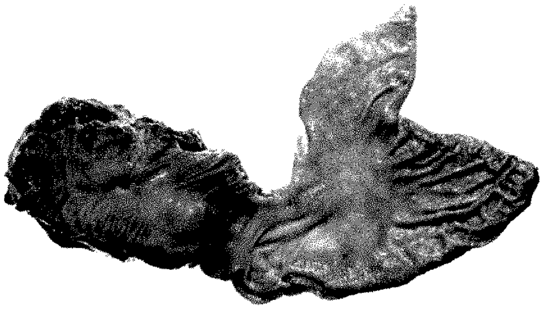


FIG. 2. Protrusion of cystadenoma into the duodenum with two acute ulcers.

in the head of the pancreas was found. A portion of this tumor could be felt protruding into the duodenum. The gallbladder was thickened, distended and contained a solitary stone. No evidence of metastases was discernible and there was no direct involvement of the colon or liver by the tumor. Preliminary dissection freed the portal vein and the superior mesenteric vessels from the tumor which was then deemed resectable. The distal portion of the stomach, the head of the pancreas, the common bile duct below the cystic duct and the duodenum to its fourth portion were removed. The cut end of the body of the pancreas was invaginated into the end of the fourth portion of the duodenum. This was accomplished by freeing this portion of the duodenum from the ligament of Treitz. An antecolic cholecystojejunostomy and gastrojejunostomy completed the reconstruction.

Clinical Course. The postoperative course was uneventful for the first 10 days except for slight confusion and some hallucination. On the second day the hematocrit was 38 per cent, the hemoglobin 11.5 gm. per 100 ml., the red blood cell count 3.98×10^6/cu.mm., the white blood cell count 7,500/cu.mm., blood urea nitrogen 49.5 mg. per cent, serum sodium 136 mEq./L., potassium 6.3 mEq./L. and chlorides 108 mEq./L. There was still some diarrhea with passage of tarry stools but the patient's condition was generally promising. On the tenth day he developed a severe shaking chill and a temperature of 103°F. The chest was clear and the abdomen was soft. The leukocyte count was 18,100/cu.mm. with 36 per cent segmented neutrophils, 46 per cent band forms, 6 per cent lymphocytes, 5 per cent monocytes and 7 per cent eosinophils. The hematocrit was 34 per cent, the hemoglobin 10.1 gm. per 100 ml. and the red blood cell count 3.2×10^6/cu.mm. The possibility of ascending cholangitis, pancreatitis and pyelonephritis, or what seemed more likely, an abscess in the operative area was considered. Several blood cultures were negative. *Proteus* species and *E. coli* were cultured from the urine. Penicillin, streptomycin, tetracycline, gantrisin and colymycin were tried during the first 10 days of chills and spiking temperature without effect. Kanamycin 0.5 gm. t.i.d. was then started and after 3 days the fever and chills began to subside. It was continued for another week as the spiking temperature gradually returned to normal. Scleral jaundice was noted after the kanamycin had been given for 3 days and this increased slightly during the next 5 days but then began to fade without discontinuance of the drug. An initial serum bilirubin of 6.2 mg. per cent (4.1 mg. per cent direct) receded to 4.2 mg. per cent (direct 2.4 mg. per cent). The diarrhea that had recurred intermittently was controlled with extract of pancreas in the form of panteric tablets. The patient was discharged 6 weeks after operation and has continued in good health since.

Pathologic Findings. The specimen consisted of stomach, duodenum and head of pancreas. There was no ulceration in the stomach. Beyond the pylorus a portion of duodenum measuring 17 cm. in length was stretched over the surface of a large cystic spherical mass 10 cm. in diameter in the head of the pancreas. Eight centimeters distal to the pylorus, there was a nodular protrusion of the mass into the lumen of the duodenum and this was covered by intact mucosa. The common bile duct opened freely into the duodenum at the ampulla of Vater and was joined here by the pancreatic duct which was

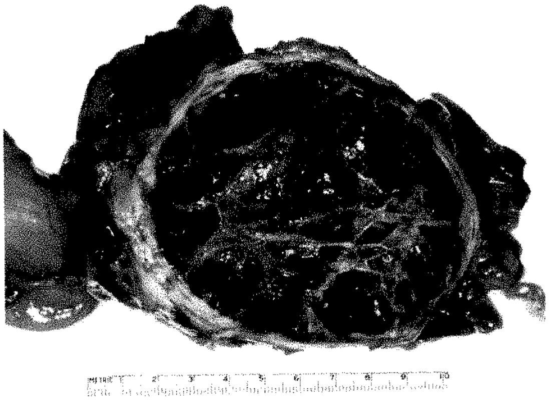


FIG. 3. Cut surface of multilocular cystadenoma.

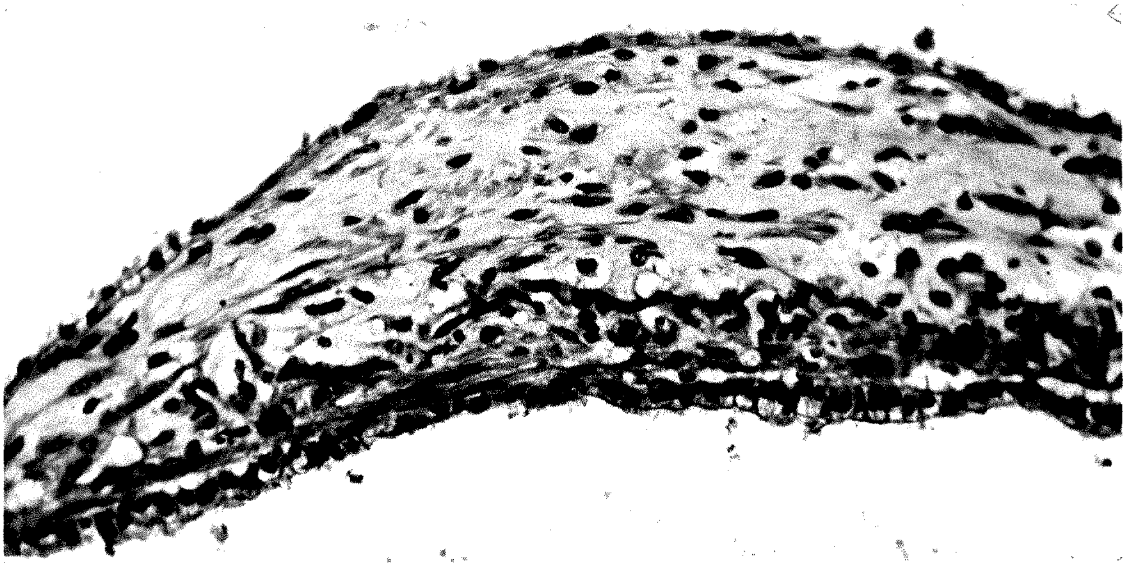


FIG. 4. Septum of tumor lined by clear cuboidal and columnar epithelial cells (H.E.×286).

dilated and displaced over the surface of the lesion. One centimeter proximal to the ampulla were two small punched out ulcers in the mucosa of the duodenum, one 2 mm. and the other 5 mm. in diameter (Fig. 2).

On sectioning the tumor there was a cystic cavity bounded by a well defined fibrous wall measuring on the average 6 mm. in thickness. The central portion consisted of very thin connective tissue trabeculae separating multilocular cysts filled with clear serous fluid. Hemorrhage had occurred into some of the cysts. There were no papillary projections although small daughter cysts were attached to the walls of the larger cysts (Fig. 3).

On microscopic examination the tumor had a thick fibrous tissue capsule. Small portions of pancreas showing compression atrophy and interstitial fibrosis of parenchymal tissue were present on the outside of the capsule. A few normal lymph nodes were also present extracapsularly. The tumor itself was composed of multiple cystic spaces formed by fibrous septa lined by epithelium which in general had a clear vacuolated cytoplasm. In some areas the epithelium was columnar with basely situated nuclei; in others the epithelium had become cuboidal and flattened from pressure of the contents (Fig. 4). Some of the cystic spaces contained clear fluid but others showed evidence of recent and old hemorrhage with erythrocytes present. Some hemosiderin-laden phagocytes were present in the septa throughout the tumor. The common bile duct and pancreatic duct were closely related to each other as they were stretched over the capsule of the tumor. Sections from the duodenum showed 2 acute ulcers in the mucosa of the duodenum, both showing evidence of recent hemorrhage. The tumor in this portion was not well encapsulated and its cystic spaces extended into the submucosa up to the muscularis mucosae beneath the ulcers (Fig. 5). The diagnosis was cystadenoma of the head of the pancreas causing two acute duodenal ulcers with recent hemorrhage.

DISCUSSION

The rarity of pancreatic cystadenomas is attested to by the scattered reports of individual cases and the few collected series of such cases. Frantz[3] finds that the number in the literature is hard to ascertain accurately. At the Presbyterian Hospital in New York City in 23,551 surgical specimens there were 10 cystadenomas, 3 multilocular and 7 papillary. Howard and Jordan[5] collected a total of 88 cases of cystadenoma from the literature up until 1960; Piper *et al.*[6] added another 20 examples in 1962, while Campbell and Cruickshank[2] reported 14 more such cases. According to Piper *et al.*,[6] cystadenomas constitute about 7 per cent of cystic lesions of the pancreas. A logical classification was proposed by Glen-

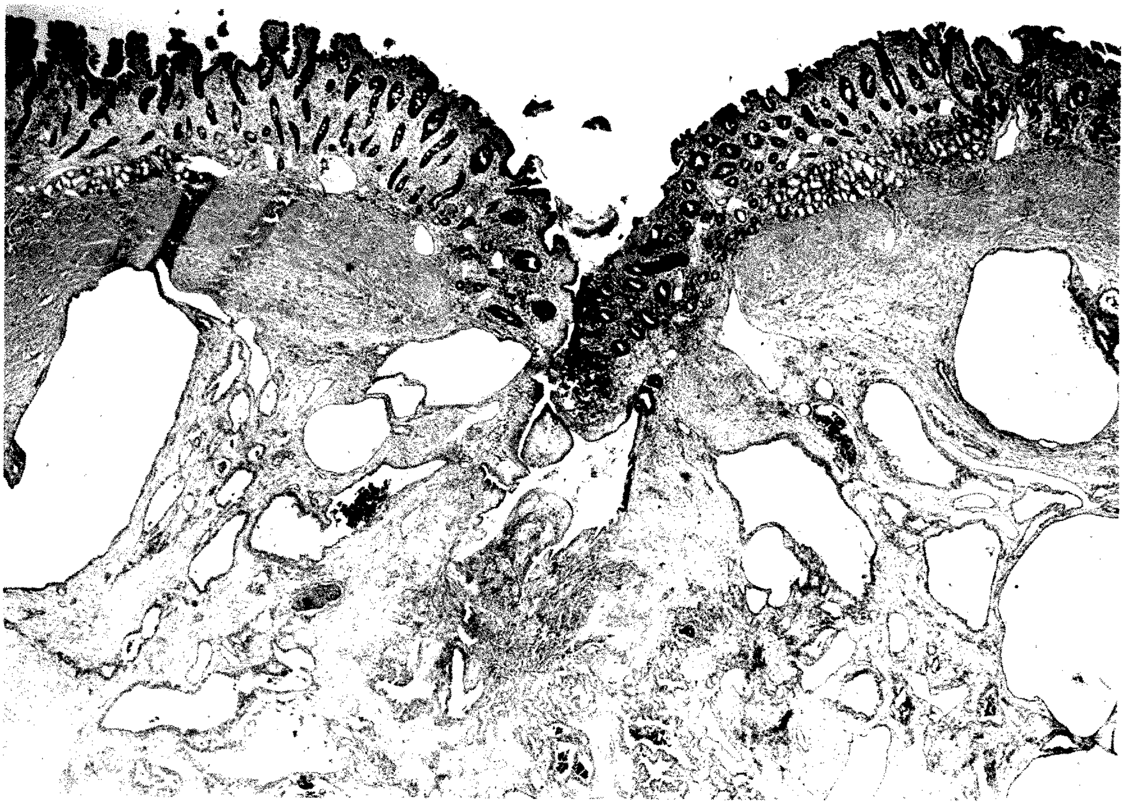


FIG. 5. Extension of cystic spaces into duodenal submucosa with associated acute ulcer (H.&E. ×23).

ner and Mallory[4] who divided their cases into simple and papillary with subclassifications of serous or mucinous.

The size of cystadenomas is variable and may reach 20 cm. or more.[3,6] By far the majority of tumors have developed in the body or tail of the pancreas. In the rarer instances where the lesion is located in the head of the pancreas, there is characteristically widening and stretching of the duodenal loop on roentgenograms. When the duodenal mucosal pattern is distorted as in our case and in 2 cases of Piper *et al.*,[6] serious consideration must be given to the diagnosis of pancreatic carcinoma. The lack of true encapsulation observed in the duodenal aspect of our case permitted the cystic spaces to extend through the muscular coat of the duodenum to the submucosa with resultant ulceration of the overlying mucosa. It is quite common to find portions of ectopic pancreatic tissue within the duodenal wall and it is therefore conceivable that the tumor may have developed from such an area. To our knowledge there is only one other report[1] of extension of a benign cystadenoma into the submucosa of the duodenum, although 3 of Piper and coworkers'[6] cases had associated duodenal ulcers. In 1 of the 2 cases with intestinal hemorrhage reported by Campbell and Cruickshank,[2] the cyst was firmly adherent to the posterior wall of the stomach.

Pain, dyspepsia and the appearance of a mass constitute the more common symptoms of pancreatic cystadenoma. The unusual problem posed initially by our patient was how to account for the severe intestinal hemorrhage and what the nature of the mass was in the right upper quadrant of the abdomen. In this effort roentgen studies were extremely helpful in pointing to the possibility of a lesion in the head of the pancreas with the added likelihood that this was malignant in view of the compression deformity of the duodenal loop and its invasion or involvement by the tumor. The possibility of a ruptured aneurysm of the abdominal aorta, however, could not be disregarded. The preoperative diagnosis was divided between these two possibilities. The findings at operation confirmed the opinion of the roentgenologist except that the lesion was benign and could be completely excised. The hemorrhage stemmed from two acute duodenal ulcers caused by local penetration of the pancreatic tumor into the duodenal wall.

SUMMARY

A patient with severe intestinal hemorrhage and an indistinct mass in the right upper quadrant of the abdomen was found at operation to have a benign cystadenoma of the head of the pancreas and two acute bleeding duodenal ulcers caused by penetration of the lesion into the duodenal wall. Complete recovery followed removal of the tumor and gastric resection (Whipple's procedure).

Cystadenoma of the pancreas is a relatively rare lesion with few clinical characteristics of its own. It may, however, manifest its presence as in the case reported here, by effect on contiguous tissues.

W. S. Reveno, M.D.
Harper Hospital
Detroit 1, Michigan

REFERENCES

1. Brunschwig, A. The Surgery of Pancreatic Tumors. C. V. Mosby Company, St. Louis, 1942, p. 179.
2. Campbell, J. A., and Cruickshank, A. H. Cystadenoma and cystadenocarcinoma of pancreas. *J. Clin. Path.*, 1962, *15*, 432–437.
3. Frantz, V. K. Atlas of Tumor Pathology. Section VII—Fasc. 27 and 28. Tumors of the Pancreas. Armed Forces Institute of Pathology, Washington, D. C., 1959.
4. Glenner, G. G., and Mallory, G. K. Cystadenoma and related nonfunctional tumors of pancreas. *Cancer*, 1956, *9*, 980–996.
5. Howard, J. M., and Jordan, G. L. Surgical Diseases of the Pancreas. J. B. Lippincott Company, Philadelphia, 1960.
6. Piper, C. E., Jr., Remine, W. H., and Priestley, J. T. Pancreatic cystadenomata; report of 20 cases. *J.A.M.A.*, 1962, *180*, 648–652.

ANNULAR PANCREAS IN INFANCY*

REPORT OF 3 CASES

By NAIM K. ATALLAH, M.D., *and* RAFIC E. MELHEM, M.D.
BEIRUT, LEBANON

ANNULAR pancreas is a congenital anomaly consisting of a band of pancreatic tissue encircling the duodenum distal to the bulb and is frequently associated with varying degrees of duodenal constriction. The number of the reported cases of annular pancreas in infants has increased greatly in the last decade, suggesting that the anomaly is more common than it was previously believed to be.

The purpose of this paper is to record our experience with 3 cases of annular pancreas in infancy encountered in the last 2 years at the American University Hospital. To our knowledge, these are the first cases reported from the Middle East.

REPORT OF CASES

CASE I. Baby K. This newborn female was found at birth to have an imperforate anus and a rectovaginal fistula. On the second postnatal day, the patient started vomiting between feedings. The vomitus was bile-stained and guaiac positive. A roentgenogram of the abdomen showed a moderately distended stomach and duodenal bulb and only a few air bubbles in the distal intestines (Fig. 1). Gastrografin examination showed a high grade stenosis of the second portion of the duodenum (Fig. 2, *A* and *B*). The possibility of an annular pancreas was suggested. At operation, the stomach and the duodenal bulb were found to be dilated; the second portion of the duodenum was constricted by a band of pancreatic tissue that encircled it. The cecum lay in the right upper quadrant. A side-to-side duodenojejunostomy was performed in a reverse peristaltic manner. Postoperatively, the patient had respiratory difficulties, and her condition deteriorated rapidly. Chest roentgenograms showed pneumonia and an enlarged heart with prominent pulmonary vessels suggesting a left-to-right shunt. The baby succumbed 2 days later from heart failure.

CASE II. N.H. This 8 month old male infant started 2 months prior to admission to vomit 15 to 30 minutes after feedings. A right inguinal hernia was noted on admission. Gastrointestinal series demonstrated a normal-sized stomach and a slightly dilated bulb. The second portion of the duodenum showed considerable narrowing, but barium flowed through it in sufficient amount to outline well the distal intestines (Fig. 3). Annular pancreas was suggested as the probable etiology.

At operation, a band of pancreatic tissue, 1 cm. wide, was found traversing the second part of the duodenum from the right to the left side. The stomach and first portion of the duodenum were dilated. A retrocolic duodenojejunostomy was performed.

The patient was re-admitted 15 months later because of signs of obstruction of 3 days' duration. A barium meal study revealed distal small bowel obstruction. At operation, adhesion bands around the midportion of the ileum were released. The patient did well postoperatively.

CASE III. Baby S. This 8 day old male infant was cyanosed at birth for a period of 1 hour. One day prior to admission, he started to vomit coffee-ground material. On admission, he was hypotonic, had a small head, deformed ear lobes and mongoloid facies. A chest roentgenogram showed pneumonia. On a plain roentgenogram of the abdomen, only the stomach and the duodenal bulb were filled with gas (Fig. 4). Barium meal studies showed the stomach to be moderately dilated, as were the pyloric canal and the duodenal bulb (Fig. 5, *A* and *B*). Six hours later, a small amount of contrast material had passed beyond the second portion of the duodenum. A postbulbar stenosis was diagnosed and the possibility of annular pancreas was suggested. At operation, it was noted that a tongue of pancreatic tissue had encircled the second portion of the duodenum and constricted it. The stomach and first portion of the duodenum were slightly dilated. A side-to-side duodenoduodenostomy bypassing the constriction was performed. Postoperatively, the patient did well.

---

* From the Department of Radiology, American University Hospital, Beirut, Lebanon.

DISCUSSION

Ecker in 1862 introduced the term "annular pancreas," and Vidal in 1905 described the first case in an infant and performed the first successful operation.

Many papers dealing extensively with the various theories of development of annular pancreas are available.[1,7,11] In brief, the pancreas develops from a dorsal and a ventral anlage budding from the primitive duodenum. The left portion of the ventral anlage ultimately atrophies, while the right portion develops and follows the clockwise rotation of the duodenum to form the lowermost part of the head of the pancreas; the remaining pancreas is derived from the dorsal anlage.

Tieken believed that annular pancreas develops as a result of hypertrophy of the right anlage, encircling the dudenum. Lecco advanced the theory that the top of the right ventral anlage becomes fixed, and with rotation of the intestine, a ring-like band is formed around the duodenum. Baldwin, on the other hand, believes that the left ventral anlage is sometimes retained and gives rise to the annulus.

The annular band is made up of normal pancreatic tissue. Occasionally, in older cases, evidence of chronic pancreatitis is seen. The anatomy of the duct system of the annulus is not constant. Out of the 19 cases reviewed by Moore[12] in 1953, 16 opened into the main pancreatic duct, 1 in the accessory pancreatic duct, 1 in the common bile duct and 1 opened separately into the duodenum.

Ravitch and Woods[14] report that in 200,000 autopsies at the Johns Hopkins Hospital, annular pancreas had not been encountered even once. Skapinker[18] states that in the cases reviewed by him, annular pancreas was missed in 5 instances at the first laparotomy. Our belief is that the anomaly is easily missed if not specifically looked for.

The condition seems to be predominant in males. Fifty out of the 64 cases collected by Kieswetter and Koop[9] in which the sex was recorded were males. The anomaly has been reported in all age groups, from a 16 mm. embryo (Weissberg) to a 74 year old patient (Custer and Waugh). The earlier reports stress a higher frequency beyond the age of 40 years. Friedman[3] in 1957, however, found that 40 out of the 86 patients operated on for annular pancreas were infants.

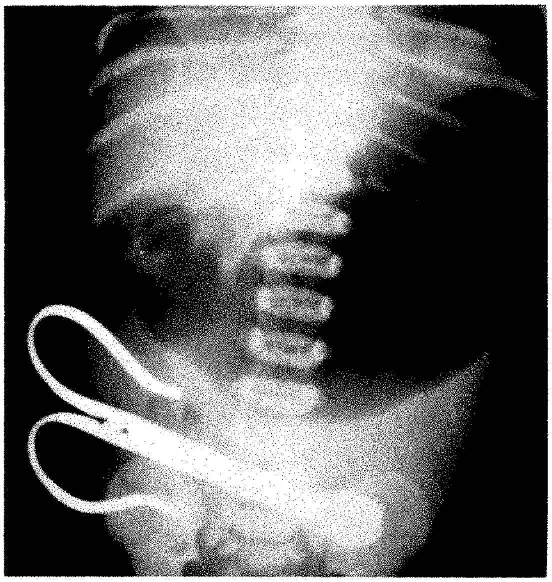


Fig. 1. Case i. Roentgenogram of the abdomen showing a moderately distended stomach and duodenal bulb and only a few air bubbles in the distal intestines.

The presenting symptoms in infancy in the majority of cases are those of high intestinal obstruction. Fourteen out of a group of 15 cases reviewed by Kieswetter and Koop[9] presented with vomiting as did our 3 cases. If the annulus causes marked or complete obstruction, symptoms develop in the neonatal period (Cases i and iii). Milder degrees of constriction cause symptoms later in life (Case ii), or not at all. The degree of epigastric distention is usually not marked, as these infants vomit and decompress their stomach and duodenum. Aspiration pneumonia is common.

Some cases present with obstructive jaundice. This is probably due to obstruction

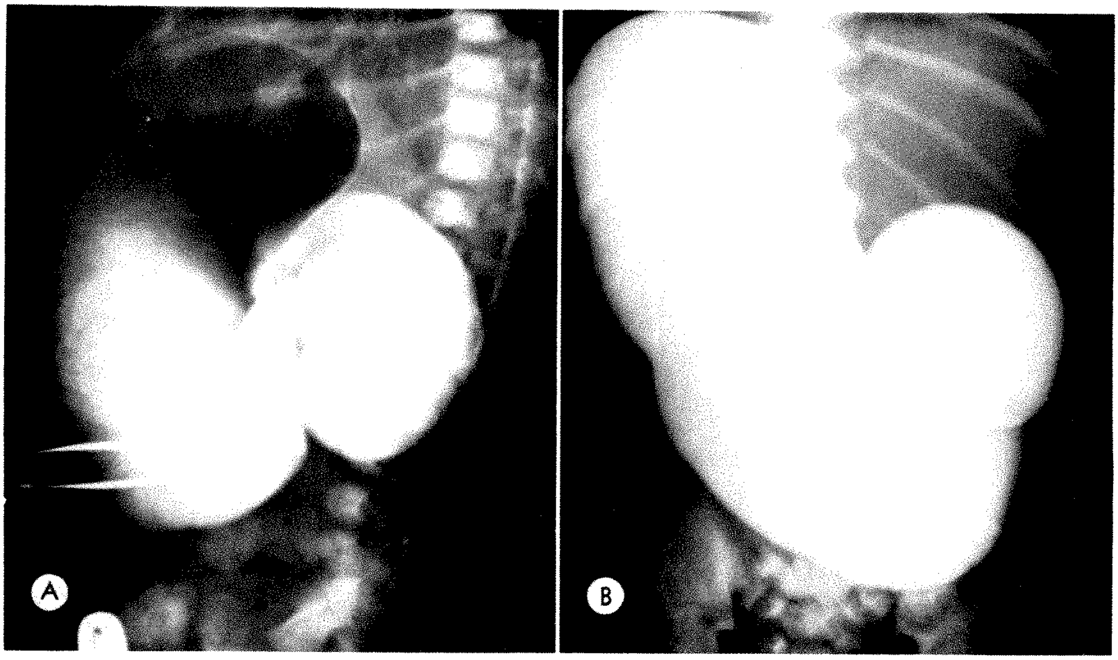


Fig. 2. Case I. (*A* and *B*) Roentgenograms showing a high grade stenosis of the second portion of the duodenum.

of the common bile duct by the annulus, or possibly due to pressure on the common bile duct by a distended duodenum.[21] Pancreatitis of the ring and of the rest of the pancreas is common, having been reported in 16 per cent of the cases.[21] A mild constriction of the duodenum could thus

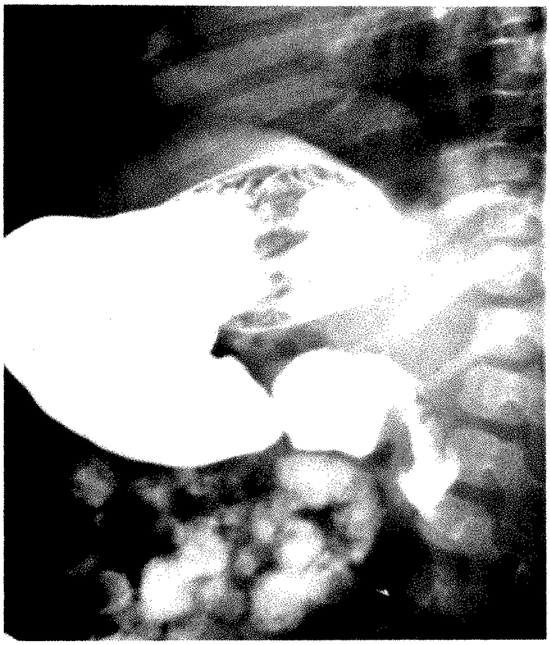


Fig. 3. Case II. Roentgenogram showing considerable narrowing of the second portion of the duodenum.

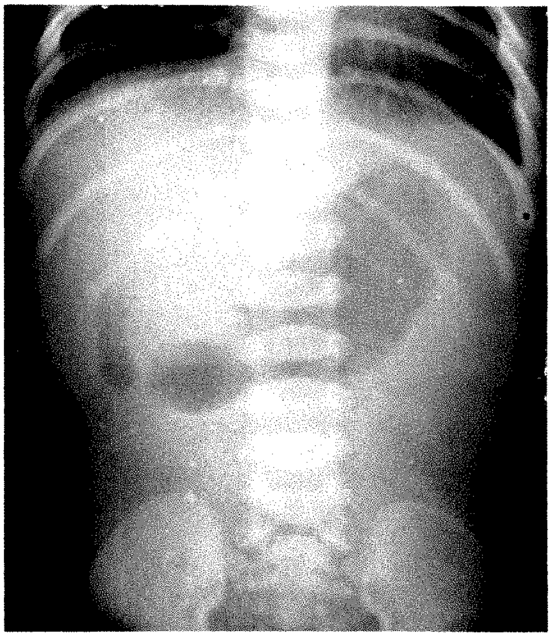


Fig. 4. Case III. Plain roentgenogram showing gas only in the stomach and duodenal bulb.

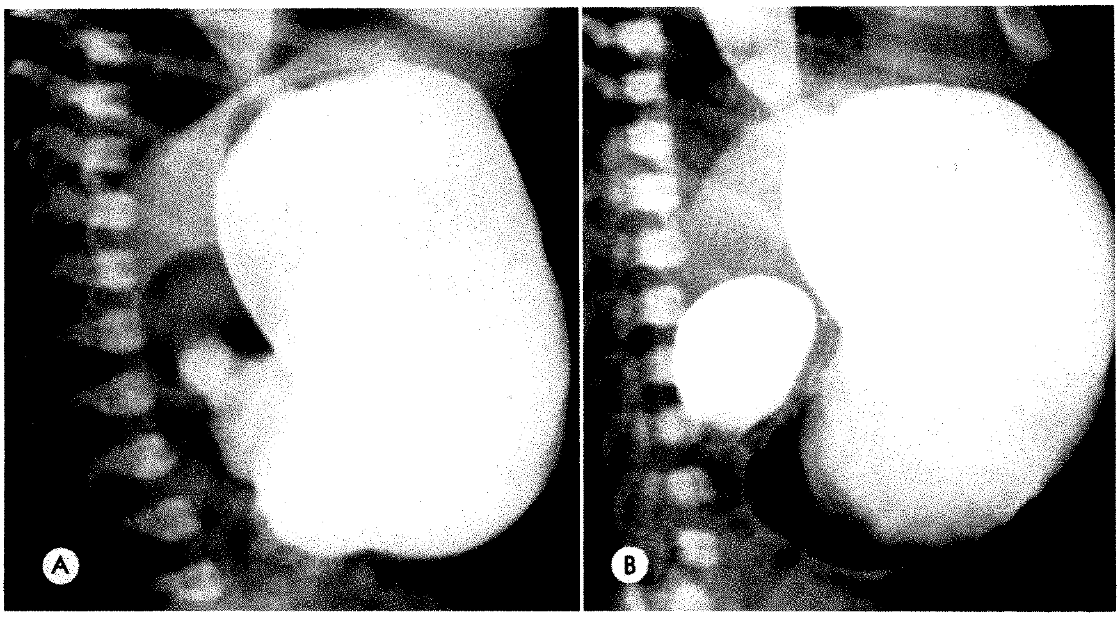


FIG. 5. Case III. (*A* and *B*) Barium meal studies showing a dilated stomach, pyloric canal and duodenal bulb.

become severe with pancreatitis and edema, and account for the late development of obstructive symptoms in older patients.

The presence of other congenital anomalies in patients with annular pancreas is well documented. Eighteen out of 24 cases in the pediatric group reviewed by Kieswetter and Koop[9] had associated anomalies, 16 of which were incompatible with life. Gross[5] reported 10 cases, 9 of which had other anomalies. Whelan and Hamilton[21] gave an incidence of 70 per cent of associated anomalies in children. Forty-three per cent of the cases of annular pancreas had associated duodenal atresia or stenosis. This suggests that one basic etiologic disturbance could be responsible for both anomalies. The other commonest associated anomalies were malrotation of the intestines (23 per cent), esophageal atresia with or without tracheoesophageal fistula (12 per cent), Meckel's diverticulum (12 per cent), congenital heart disease (12 per cent), and mongolism (12 per cent). Several of the cases presented with more than one congenital anomaly. One of our cases (Case I) had such multiple anomalies. Another had an inguinal hernia (Case II) and the third was a mongol (Case III).

If in a neonate a plain roentgenogram of the abdomen shows an air-filled stomach and duodenal bulb, the so-called double-bubble sign, and no gas distal to the second portion of the duodenum, a complete obstruction at the site can be assumed. The possibility of annular pancreas should be entertained, but can be confirmed only at operation. The use of liquid contrast media in such cases is unnecessary and may be dangerous because of liability of vomiting and aspiration. The use of positive contrast media is essential in the presence of partial obstruction for the proper evaluation of the degree, location and extent of the constricted segment. The information gained is often helpful in differentiating the condition from duodenal stenosis and bands. It is also desirable to take delayed roentgenograms in order to locate the cecum and rule out a mobile cecum and malrotation.

Mast, Telle and Turek[10] describe 3 roentgenologic criteria which are helpful in the diagnosis of annular pancreas. These are: (1) a smooth, annular filling defect of the second and occasionally the third portion of the duodenum; (2) the varying degree of symmetric dilatation of the duodenum proximal to the constriction; and (3) a fluoroscopic evidence of reversed peristalsis present at the duodenum proximal to the obstruction. (This latter finding is present in cases of more advanced degree of obstruction.) Poppel[13] emphasizes alteration atrophy of the character of the valvulae conniventes in the affected segment.

Early cases were treated by a simple division or resection of the ring. However, pancreatitis and pancreatic fistula formation have been particularly troublesome complications. In addition, the high incidence of duodenal atresia or stenosis in cases with annular pancreas necessitates a bypass type of operation. Also, in some cases the annulus is so deeply embedded in the wall of the duodenum that to section the annulus one must almost enter the duodenum.

Most workers consider isoperistaltic duodenojejunostomy, antecolic or retrocolic, to be the procedure of choice in infants, since it bypasses the constriction, it does not involve cutting through pancreatic tissue, no gastric resection is performed and the danger of the development of a stomal ulcer is not present. However, Mast, Telle and Turek[10] have reviewed the cases treated in this manner and found that the dilated stomach of an infant may fail to regain normal tone, and persistent dilatation and malfunction of the stoma often occur. They believe that the proximal duodenum may not be sufficiently dilated for the performance of a quick anastomosis and that the mobilization of the duodenum may precipitate shock in an infant. In view of these findings, the authors state that the preferred technique in an infant would seem to be a gastroenterostomy.

CONCLUSION AND SUMMARY

Annular pancreas is a common enough anomaly to be seriously considered in the differential diagnosis whenever an infant presents with symptoms of high intestinal obstruction. Three cases of annular pancreas in infancy are reported. In such instances one or several other associated congenital anomalies are often noted. The majority of the cases present with high intestinal obstruction. A roentgenologic diagnosis is often possible.

Naim K. Atallah, M.D.
Department of Radiology
American University Hospital
Beirut, Lebanon

We wish to thank Drs. H. Mishalany and S. Obeid for the case material, and Dr. M. LeMay for her helpful criticism.

REFERENCES

1. Arey, L. B. Developmental Anatomy: a Textbook and Laboratory Manual of Embryology. Fifth edition. W. B. Saunders Company, Philadelphia, 1946.
2. Boothroyd, L. S. A. Annular pancreas. *Ann. Surg.*, 1957, *146*, 139–144.
3. Friedman, A. I. Annular pancreas: congenital abnormality manifest in aged. *Gastroenterology*, 1957, *32*, 1172–1177.
4. Gilroy, J. A., and Adams, A. B. Annular pancreas. *Radiology*, 1960, *75*, 568–571.
5. Gross, R. E. The Surgery of Infancy and Childhood: Its Principles and Techniques. W. B. Saunders Company, Philadelphia, 1953, pp. 204–210.
6. Hope, J. W., and Gibbons, J. F. Duodenal obstruction due to annular pancreas with differential diagnosis of other congenital lesions producing duodenal obstruction. *Radiology*, 1954, *63*, 473–488.
7. Howard, N. J. Annular pancreas. *Surg., Gynec. & Obst.*, 1930, *50*, 533–540.
8. Kie, A. T., Wittebol, P., and Lunding, J. Annular pancreas. *Acta Paediat.*, 1961, *50*, 72–79.
9. Kieswetter, W. B., and Koop, C. E. Annular pancreas in infancy. *Surgery*, 1954, *36*, 146–159.
10. Mast, W. H., Telle, L. D., and Turek, R. O. Annular pancreas: errors in diagnosis and treatment of eight cases. *Am. J. Surg.*, 1957, *94*, 80–89.
11. McNaught, J. B. Annular pancreas: compilation of 40 cases, with report of new case. *Am. J. M. Sc.*, 1933, *185*, 249–260.
12. Moore, T. C. Annular pancreas: review of literature and report of two infant cases. *Surgery*, 1953, *33*, 138–148.
13. Poppel, M. H. Roentgen Manifestations of Pancreatic Disease. Charles C Thomas, Publisher, Springfield, Ill., 1951, pp. 12–15.

14. Ravitch, M. M., and Woods, A. C., Jr. Annular pancreas. *Ann. Surg.*, 1950, *132*, 1116–1127.
15. Sanford, C. E. Annular pancreas as surgical problem. *A.M.A. Arch. Surg.*, 1955, *71*, 915–926.
16. Shapiro, D. J., Dzurick, F. J., and Gerrish, E. W. Obstruction of duodenum in newborn due to annular pancreas. *Pediatrics*, 1952, *9*, 764–772.
17. Singleton, E. B. X-Ray Diagnosis of the Alimentary Tract in Infants and Children. Year Book Publishers, Inc., Chicago, 1959, pp. 184–189.
18. Skapinker, S. Annular pancreas. *J. Internat. Coll. Surgeons*, 1954, *22*, 414–421.
19. Swynnerton, B. F., and Tanner, N. C. Annular pancreas. *Brit. M. J.*, 1953, *1*, 1028–1029.
20. Van der Horst, von P. L. F. Annular pancreas. *A.M.A. Arch. Surg.*, 1961, *83*, 249–252.
21. Whelan, T. J., Jr., and Hamilton, G. B. Annular pancreas. *Ann. Surg.*, 1957, *146*, 252–262.

DERMATOMYOSITIS WITH SIGNIFICANT INVOLVEMENT OF THE GASTROINTESTINAL TRACT

By FRIEDA FELDMAN, M.D., *and* RICHARD H. MARSHAK, M.D.
NEW YORK, NEW YORK

IN MOST articles on dermatomyositis, attention has been centered on the clinical aspects and histopathologic features of the skin and muscle lesions. Although rare comments on changes in the gastrointestinal tract have been made, early authors regarded these as incidental to the disease process and in several large reported series no reference is made to the gastrointestinal tract. Roentgen changes, in particular, were infrequently mentioned and with one exception[34] we were unable to find any report in which illustrative roentgenograms were used to show that dermatomyositis may change the appearance of the intestinal tract.

It is our purpose to present a case of dermatomyositis with marked gastrointestinal involvement documented by roentgen examination.

REVIEW OF THE LITERATURE

The earliest recorded case of dermatomyositis was that described by Wagner[35] in 1863. In 1932, Karelitz and Welt[17] suggested that the gastrointestinal changes, rather than being incidental, were a part of the diffuse disease process. Although many case reports have since appeared in the literature,[5,6,8,16,19,21–26,30,31,33,36,37] in only a few were the findings in the gastrointestinal tract discussed.

In 1949, Wainger and Lever[36] reported 3 cases of dermatomyositis, 1 of which, a 54 year old woman, had roentgenograms of the gastrointestinal tract made prior to demise. These showed the presence of dilatation, gross segmentation, mucosal irregularities, and loss of mucosal pattern throughout the small bowel. There was also a slight delay in transit through the small intestine.

In 1952, Cottel,[6] emphasizing the association of dermatomyositis and malignancy, presented 2 cases of which a brief description of the roentgenographic findings was given. In 1 of the cases, that of a 50 year old white male who complained of hoarseness and difficulty in swallowing, roentgenograms demonstrated that the valleculae filled unusually well with barium and retained it for some time. The esophagus appeared normal. Three months later reexamination revealed retention in the valleculae, distention of the esophagus, and a large filling defect in the antrum of the stomach which subsequently proved to be a carcinoma. No mention of either the small or large bowel was made. The roentgen findings in the second case with the exception of retention of barium in the valleculae were not remarkable.

In 1953, DeGraciansky,[8] in a discussion of 6 cases of dermatomyositis, mentioned roentgen findings pertinent to the gastrointestinal tract in 4 of them. The roentgen findings were limited to reflux of barium through the nose at the moment of deglutition and marked dilatation of the colon. Gastrointestinal symptomatology included dysphagia, nausea, vomiting, epigastric pain and diarrhea. In 1956, Malkinson and Rothman[23] reported 2 cases; in 1 there was diminished peristalsis and a delayed transit time in the esophagus.

The one case of dermatomyositis that we could find in the literature with roentgen documentation was that reported by Viterbo *et al.*[34] Their case was a 23 year old white female in whom there was widening and dilatation of the duodenal sweep as well as a loss of the normal mucosal pattern and delay in emptying. In addition, dilatation, atony and delay of emptying were noted in the jejunum.

Hale and Schatzki,[14] in discussing the roentgen changes in the gastrointestinal tract in scleroderma, included 2 cases with associated dermatomyositis. Goetz'[13] case was also reported primarily as one of scleroderma although some of the histologic features resembled those of dermatomyositis.

ETIOLOGY

The etiology of dermatomyositis is unknown. It was originally considered to be a nonsuppurative inflammation of the striated muscle accompanied by cutaneous changes.[22,37] Other concepts included infection[26,31] and either an immunologic or hypersensitivity type of reaction.[6,20] At the present time, inflammation is not considered to be the primary alteration[27,36] and it has been classified by some investigators as a collagen disorder similar to scleroderma. Since many of the pathologic findings in dermatomyositis and scleroderma are similar, some authors[7,11,12,21] have considered these disorders as a single entity. Others,[4,18,19] however, believe the diseases are distinct, particularly in the advanced phase when the clinical picture becomes characteristic.

PATHOLOGIC FINDINGS

Only those pathologic findings related to the gastrointestinal tract will be emphasized. The gross morphologic alterations in the gastrointestinal tract include thickening, distention and edema of the bowel wall with serosal fibrino-purulent exudate and free peritoneal fluid. The mucosa is congested and its continuity is interrupted by numerous punched out or irregular ulcers, ranging in diameter from 3 mm. to 2 cm., which may be shallow or involve the entire bowel wall with resulting hemorrhage or perforation. Ulcerations have been described involving the entire gastrointestinal tract.[17,23,24,25,36]

Histologic changes besides mucosal erosion and ulceration include thickening and edema of the submucosa and degeneration and atrophy of the muscular coats with subsequent fibrosis. The connective tissue apparently reacts with an increase in ground substance which is associated with or followed by infiltration with lymphocytes and plasma cells. There may be fibrinoid degeneration followed by conversion of the deposited material into a filmy mesh staining like collagen with ultimate sclerosis.[10,28,29]

CLINICAL FINDINGS

Dermatomyositis is a generalized disease process involving many organs of the body with numerous clinical manifestations. One of the earliest complaints is muscular weakness. Later, extensive muscular atrophy, particularly in the upper arm and shoulder girdle, occurs with accompanying creatinuria.[10,30] Deposits of calcium may be found in the muscle fascia and subcutaneous tissue.

The most frequent complaint referable to the gastrointestinal tract is dysphagia, which has been attributed to primary involvement of the pharyngeal musculature.[23] With more widespread intestinal involvement, crampy abdominal pain, alternating constipation and diarrhea, vomiting and occult or gross blood in the stools and even massive hemorrhage have been described.

REPORT OF A CASE

A 40 year old white female presented with a chief complaint of dysphagia, abdominal distention, constipation and progressive muscular weakness. She had the usual childhood diseases including bronchopneumonia at the age of 9. Since childhood, cold or damp weather made her digits turn blue or white.

Development was normal. She was an active participant in sports. There was an uneventful pregnancy at the age of 22 with delivery of a normal female infant. After pregnancy, she developed frequent and severe "heartburn" which was diagnosed as a "dropped stomach."

In the summer of 1952, at the age of 30, she noted that she no longer could run quickly. Her legs began to tire easily and she experienced difficulty in walking and then climbing stairs. Between 1953 and 1955, these symptoms became progressively worse. Weakness, until then only evident in her legs and back, spread to the arms and shoulders. By 1956, getting out of bed became a major physical effort and sitting up after being flat could only be accomplished with assistance. Coughing and sneezing was difficult and spontaneous motion with the arms became limited. In 1957, falling became impossible to control and she sustained several minor injuries. Later that year, precipitate urination and constipation developed. In 1960 her heartburn increased and was now associated with vomiting and marked constipation.

Her family history was noncontributory. A brother, aged 31, was alive and well.

Physical examination revealed a thin, emaciated woman with generalized hyperpigmentation of the skin, especially over those areas exposed to sunlight. There was no distinctive rash. The skin of the palms and over the upper forearms was moderately thickened. Both hands showed evidence of vascular insufficiency and there were marked vasospastic color changes present. No tenderness could be elicited except at the tip of the left middle finger.

Marked wasting of the muscles of the neck, shoulder girdle, trunk and pelvic girdle was apparent. There was no sensory impairment. The tendon reflexes were equal and active.

The thyroid gland was not enlarged. The abdomen was markedly protuberant. The liver and spleen were not palpated. There was no lymphadenopathy.

The patient exhibited a waddling gait and used a rocking motion when getting out of a chair. She first threw her trunk forward and then leaning on the arms of the chair, pushed herself from side to side until the erect position was assumed. She was unable to raise herself from a supine position unless she turned on her abdomen and then used her hands to climb up on her thighs. Abduction of the arms was impossible.

The laboratory findings, including urinalysis, complete blood count, erythrocyte sedimentation rate, blood urea nitrogen, serum transaminase, liver profile, SGOT, SGPT, urinary porphyrins and 17 ketosteroid excretion, were within normal limits. Several lupus erythematosus preparations, complement fixation, latex and sensitized sheep cell studies were all negative. Serum sodium was 140 mEq./l., serum potassium 2.6 mEq./l. A 24 hour urine creatinine of 0.56 gm. was low (normal between 1.0 and 1.5 gm.) with a marked increase in creatine excretion (533 gm.) during the same period (normal less than 200 gm.). The protein bound iodine was questionable at 6.7 mg. per cent.

Biopsies from a thickened area of skin over the right third metacarpal head, skin of the right forearm and muscle and subcutaneous tissue of the right forearm were reported as showing intact epithelium. The collagen of the dermis was thick and had increased vascularity. There were numerous small capillaries at all levels, most of which had small numbers of lymphocytes around them. Sections of voluntary striated muscle showed atrophy and degeneration of muscle fibers with small accumulations of sarcolemma nuclei. The diagnosis was chronic dermatitis and chronic myositis of voluntary striated muscle consistent with dermatomyositis.

Roentgenograms of both hands showed slight prominence of the soft tissues with calcifications adjacent to the ungual tufts. A roentgenogram of the chest revealed no abnormality.

Roentgenologic investigation of the gastrointestinal tract revealed minimal dilatation of the esophagus with a slight delay in the passage of barium into the stomach. A tiny sliding hiatus hernia was present. The stomach varied in size depending upon the amount of barium that was ingested, demonstrating the fact that it was markedly atonic. Peristaltic activity was not identified. A moderate amount of secretions was present. No organic filling defects were seen (Fig. 1).

The duodenal bulb was normal. The second and third portions of the duodenum were markedly dilated (Fig. 1, 2 and 3). Throughout the entire fluoroscopic examination, practically no barium entered the small intestine and throughout a period of 6 hours, very little of the barium passed distal to the ligament of Treitz (Fig. 2). At the end of 8 hours, there was still visualization of only a few loops of proximal jejunum which were dilated and contained a moderate amount of secretions. The remainder of the small bowel could only be intermittently studied because of the slow emptying and revealed slight segmentation, slight dilatation and a moderate amount of increased secretions. At the end of 24 hours, there was still 80 per cent retention of barium within the stomach (Fig. 3). At the end of 5 days (at which time a barium enema study was made), some barium was still identified in the stomach and in the markedly dilated second and third portions of the duodenum (Fig. 4).

Barium enema examination revealed a markedly redundant colon with slight dilatation. There was no evidence of organic filling defects and no inflammatory process could be identified. At this time, the patient was seen by several surgeons who considered the possibility of a mechanical obstruction at the ligament of Treitz. The roentgenologic impression, however, was that the findings were similar to those seen in scleroderma and suggested a marked atony rather than an organic obstruction.

After the institution of a medical regimen including potassium chloride supplements with instructions for more frequent smaller feedings, nightly aspirations of gastric residue (which ranged between 1,000 to 2,000 cc.) and colonic lavage, the patient was symptomatically improved. This improvement was only temporary. The patient went gradually downhill and succumbed 18 months later. Necropsy was not performed.

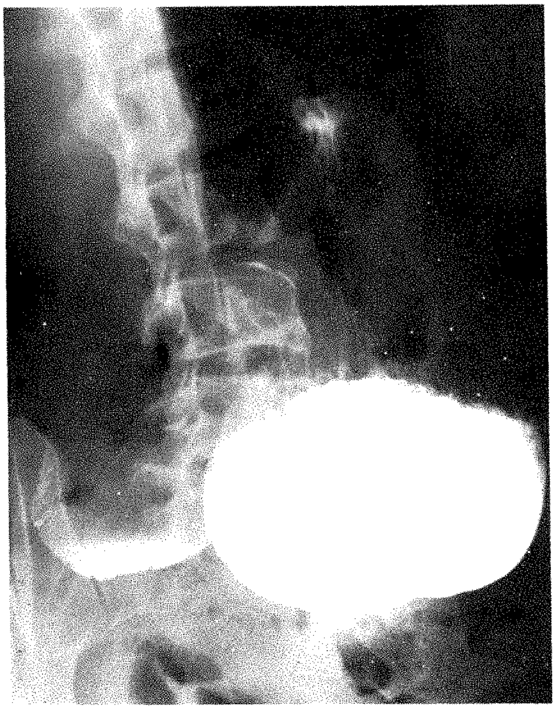


Fig. 1. Roentgenogram shows a large, atonic, ptotic stomach with retained secretions extending into the pelvis. The duodenum contains a small amount of barium and appears markedly dilated.

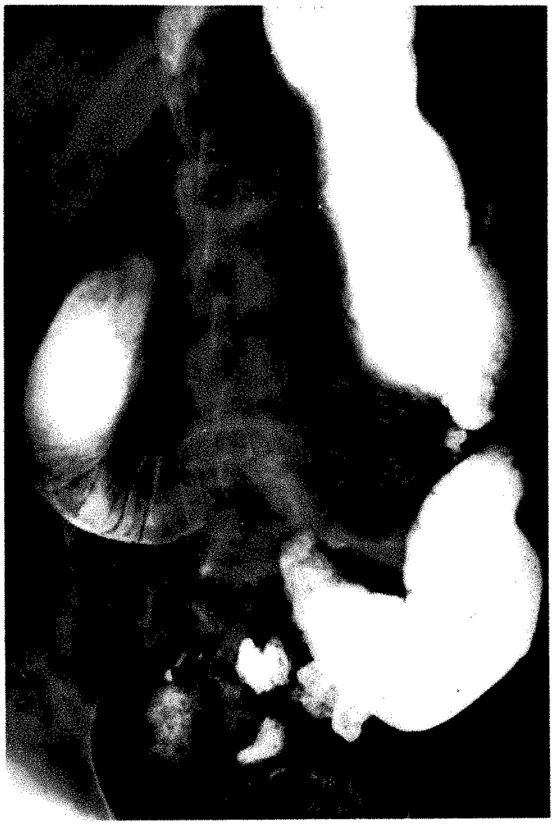


Fig. 2. Six hours post ingestion of barium, the stomach still contains the major portion of the barium meal. The second and third portions of the duodenum are dilated and the mucosal folds appear stretched and somewhat effaced. There is clumping and segmentation of the barium distally and dilatation of a loop of proximal jejunum.

DISCUSSION

Pathologic involvement of the entire alimentary tract may occur in dermatomyositis with roentgen changes.

Disturbances of deglutition may be manifested by regurgitation of barium through the nose or retention in the valleculae.[6,8,30] Initiating swallowing, particularly in the recumbent position, may be difficult. The esophagus may show moderate dilatation with significant diminution of peristalsis. Although histologic changes such as erosions and ulcerations have occurred in the esophagus,[22,23,24,36] narrowing or stricture formation has not been described. Hiatus hernias have not been significant.

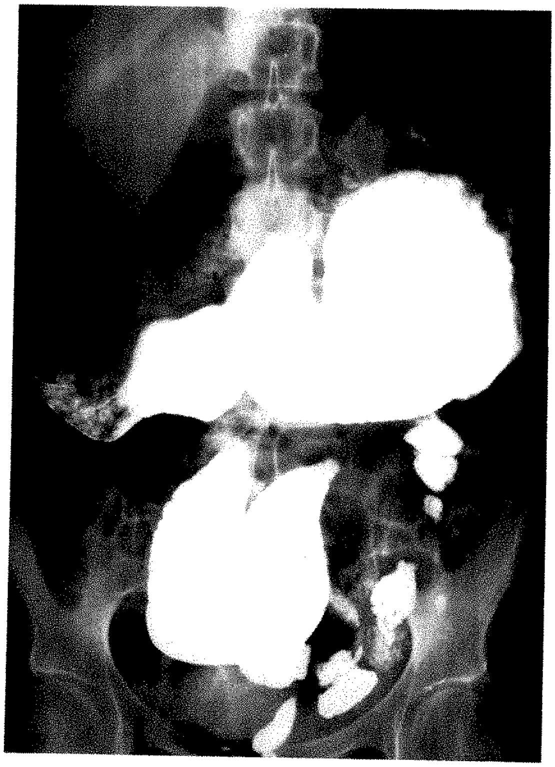


FIG. 3. At the end of 24 hours, roentgenogram shows 80 per cent retention of the barium within the stomach, dilatation of the duodenum and a dilated loop of proximal jejunum associated with segmentation.

Varying degrees of atonicity and gastric distention may be present with peristalsis being diminished or completely absent.

Roentgen changes in the small bowel are the most striking. The caliber of the bowel may be such as to suggest segmental ileus or small bowel obstruction. The hypomotility causing the prolonged transit time may be so severe that a bolus of barium entering the involved loop may remain there for hours, days or even weeks. In our case this was so marked that a duodenal residue was present for 9 days. A contributing factor may be arteriomesenteric occlusion of the third portion of the duodenum (superior mesenteric artery syndrome). This is further accentuated by the marked weakness of the abdominal wall musculature resulting in aggravation of the visceroptosis and traction on the root of the small intestinal mesentery. These features in combination with the decreased muscular tone, diminished peristalsis and hypomotility may also be responsible for the marked changes in the stomach and duodenum. The remainder of the small bowel shows varying degrees of dilatation and segmentation.

The colon may reveal varying degrees of dilatation, sacculation, and fecoliths may or may not be present. Incomplete evacuation is a frequent finding.

In general, the findings are essentially similar to those seen in scleroderma. In contrast to scleroderma, however, the esophageal changes reported in the literature and in our case were minimal. The roentgen changes in the small bowel are practically indistinguishable from those of scleroderma.

Some authors contend that scleroderma and dermatomyositis may be distinguished on a clinical basis, particularly in the advanced stages.[4] Two significant features

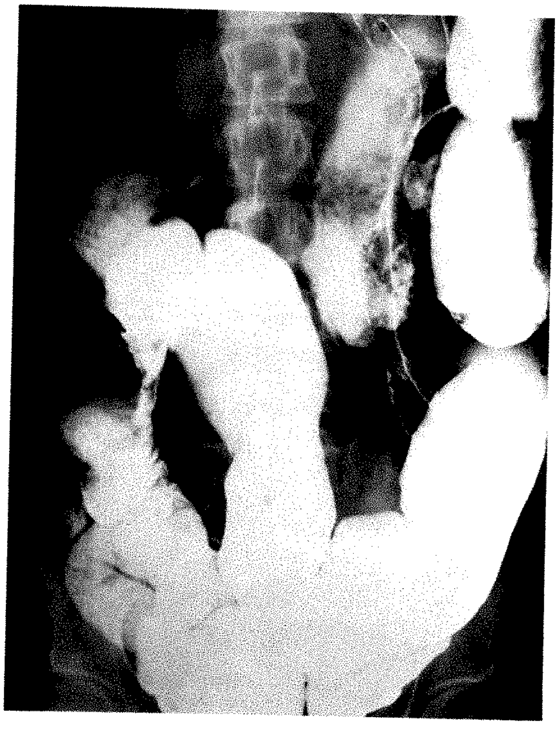


FIG. 4. Barium enema study 5 days later shows a markedly redundant, slightly dilated colon. There is ptosis of the transverse colon. Residual barium is still seen in the stomach and duodenum.

associated with dermatomyositis are the high incidence of malignancy and the extremely rapid course culminating in early death. The mortality rate in several reported series of cases of dermatomyositis was 50 per cent[10,24,30] and the duration of activity of the disease averaged 5 years. Malignant visceral growths occur in patients with dermatomyositis more frequently than in the general population.[5,6,30] The tumors have usually been detected at some time after the signs and symptoms of dermatomyositis have become apparent and the relationship of the two conditions has been further reinforced by the observation of clinical improvement in the dermatomyositis following extirpation of the tumor.[3,5,23]

No correlation between the extent of skin changes and skeletal disability and the degree of intestinal involvement could be found. Roentgen changes may precede clinical signs and, particularly, disturbances of motility may precede detectable organic changes by many years.[7] Although the early roentgen manifestations may be regarded as functional rather than anatomic, they may serve as an adequate basis for the frequent complaints of regurgitation, dysphagia, nausea, vomiting, bloating, distention and constipation causing progressive interference with nutrition.

SUMMARY

A patient with dermatomyositis showing marked changes of the gastrointestinal tract is reported. The roentgen findings included pronounced dilatation of the stomach and of the second and third portions of the duodenum associated with hypomotility and simulated and organic obstruction. The differential features are discussed.

Richard H. Marshak, M.D.
1075 Park Avenue
New York 28, New York

REFERENCES

1. Abrams, H. L., Carnes, W. H., and Eaton, J. Alimentary tract in disseminated scleroderma with emphasis on small bowel. *A.M.A. Arch. Int. Med.*, 1954, *94*, 61–81.
2. Banks, B. M. Is there a common denominator in scleroderma, dermatomyositis, disseminated lupus erythematosus, Libman-Sacks syndrome and polyarteritis nodosa? *New England J. Med.*, 1941, *225*, 433–444.
3. Bezecny, R. Dermatomyositis. *Arch. Dermat. u. Syph.*, 1935, *171*, 242–251.
4. Brock, W. G. Dermatomyositis and diffuse scleroderma; differential diagnosis and reports of cases. *A.M.A. Arch. Dermat. & Syph.*, 1934, *30*, 227–240.
5. Brunner, M. J., and Lobraico, R. V., Jr. Dermatomyositis as index of malignant neoplasm: report of case and review of literature. *Ann. Int. Med.*, 1951, *34*, 1269–1273.
6. Cottel, C. E. Dermatomyositis and malignant neoplasm. *Am. J. M. Sc.*, 1952, *224*, 160–168.
7. Cullinan, E. R. Scleroderma (diffuse systemic sclerosis). *Proc. Roy. Soc. Med.*, 1953, *46*, 507–511.
8. deGraciansky, P. Remarques à propos de six cas de dermatomyosite. *Semaine hôp. Paris*, 1953, *29*, 1621–1633.
9. Dowling, G. B., and Griffiths, W. J. Dermatomyositis and progressive scleroderma. *Lancet*, 1939, *1*, 1424–1428.
10. Ehrich, W. E. Nature of collagen diseases. *Am. Heart J.*, 1952, *43*, 121–156.
11. Freudenthal, W. Generalized scleroderma and dermatomyositis: histological comparison. *Brit. J. Dermat.*, 1940, *52*, 289–295.
12. Friedman, E. D. Dermatomyositis. *M. J. & Record*, 1926, *123*, 382–386.
13. Goetz, R. H. Pathology of progressive systemic sclerosis (generalised scleroderma) with special reference to changes in viscera. *Clin. Proc.*, 1945, *4*, 337–392.
14. Hale, C. H., and Schatzki, R. Roentgenological appearance of gastrointestinal tract in scleroderma. Am. J. Roentgenol. & Rad. Therapy, 1944, *51*, 407–420.
15. Harper, R. A. K. Radiological manifestations of diffuse systemic sclerosis (scleroderma). *Proc. Roy. Soc. Med.*, 1953, *46*, 512–522.
16. Jacoby, G. W. Subacute progressive polymyositis. *J. Nerv. & Ment. Dis.*, 1888, *15*, 697–726.
17. Karelitz, S., and Welt, S. K. Dermatomyositis. *A.M.A. Am. J. Dis. Child.*, 1932, *43*, 1134–1149.
18. Keil, H. Dermatomyositis and systemic lupus erythematosus. II. Comparative study of essential clinicopathologic features. *A.M.A. Arch. Int. Med.*, 1940, *66*, 339–383.
19. Kinney, T. D., and Maher, M. M. Dermatomyositis; study of five cases. *Am. J. Path.*, 1940, *16*, 561–594.
20. Klemperer, P. Concept of collagen diseases. *Am. J. Path.*, 1950, *26*, 505–519.

21. Langmead, F. S. Relationship between certain rare diseases: generalized scleroderma, calcinosis, dermatomyositis, myositis fibrosa. *Arch. Pediat.*, 1923, *40*, 112–120.

22. Lewy, R. B. Dermatomyositis and scleroderma; unusual causes of dysphagia. *A.M.A. Arch. Otolaryng.*, 1950, *52*, 31–39.

23. Malkinson, F. D., and Rothman, S. Changes in gastrointestinal tract in scleroderma and other diffuse connective tissue diseases. *Am. J. Gastroenterology*, 1956, *26*, 414–432.

24. Marcus, I. H., and Weinstein, J. Dermatomyositis; report of case with review of literature. *Ann. Int. Med.*, 1935, *9*, 406–425.

25. Moore, C., and Koch, L. A. Dermatomyositis; report of case with necropsy. *A.M.A. Am. J. Dis. Child.*, 1928, *35*, 71–81.

26. O'Leary, P. A., and Waisman, M. Dermatomyositis; study of forty cases. *A.M.A. Arch. Dermat. & Syph.*, 1940, *41*, 1001–1019.

27. Pagel, W., and Treip, C. S. Viscero-cutaneous collagenosis; study of intermediate forms of dermatomyositis, scleroderma, and disseminated lupus erythematosus. *J. Clin. Path.*, 1955, *8*, 1–18.

28. Pagel, W., Woolf, A. L., and Asher, R. Histological observations on dermatomyositis. *J. Path. & Bact.*, 1949, *61*, 403–411.

29. Pagel, W. Polyarteritis nodosa and "rheumatic diseases." *J. Clin. Path.*, 1951, *4*, 137–157.

30. Sheard, C., Jr. Dermatomyositis. *A.M.A. Arch. Int. Med.*, 1951, *88*, 640–658.

31. Stuckey, E. S. Dermato-myositis: summary of literature and report of case with commentary. *Brit. J. Dermat.*, 1935, *47*, 85–109.

32. Talbott, J. H., Gall, E. A., Consolazio, W. V., and Coombs, F. S. Dermatomyositis with scleroderma, calcinosis and renal endarteritis associated with focal cortical necrosis. *A.M.A. Arch. Int. Med.*, 1939, *63*, 478–496.

33. Unverricht, H. Polymyositis acuta progressiva. *Ztschr. klin. Med.*, 1887, *12*, 533–549.

34. Viterbo, F., Albano, O., and Cavallo, A. Radiological aspects of small intestine in collagen diseases. (C) Small intestine in scleroderma and in dermatomyositis. *Arch. ital. mal. app. diger.*, 1960, *27*, 162–175.

35. Wagner, E. Fall einer seltenen Muskelkrankheit. *Arch. f. Heilkunde*, 1863, *4*, 282–283.

36. Wainger, C. K., and Lever, W. F. Dermatomyositis; report of three cases with postmortem observations. *A.M.A. Arch. Dermat. & Syph.*, 1949, *59*, 196–208.

37. Wedgwood, R. J. P., Cook, C. D., and Cohen, J. Dermatomyositis; report of 26 cases in children with discussion of endocrine therapy in 13. *Pediatrics*, 1953, *12*, 447–466.

* * *

ADENOMA OF THE DUODENAL BULB*

A CASE REPORT

By CARL W. BOYER, Jr., MAJOR, MC, USA,† *and* RICHARD B. HELFRICH,
MAJOR, MC, USA‡
HONOLULU, HAWAII

CASES of benign tumors of the duodenum are uncommon and when encountered have been considered worthy of being reported. Adenomas constitute the majority of these benign lesions.[1] They are usually small and pedunculated and are discovered as incidental findings on upper gastrointestinal examinations, at surgery, or at autopsy. The following case report was prompted because of the distinctly unusual roentgenographic findings produced by an uncommonly large duodenal neoplasm.

REPORT OF A CASE

A 54 year old Caucasian male was admitted to Tripler General Hospital on October 2, 1962 for an exploratory laparotomy. He had reported to his dispensary early in September because of intermittent sharp pains in the right posterior chest. For 6 months prior to admission he had noticed burning pains in this area with strenuous activity or with sneezing and coughing. The symptoms had no relation to food intake. Physical examination was negative except for a palpable liver edge 2 cm. below the right costal margin.

An anteroposterior supine roentgenogram of the abdomen taken at the dispensary revealed a 7 cm. circular soft tissue density in the right upper quadrant (Fig. 1). It was thought that the density might represent merely a normal gastric antrum. An oral cholecystogram (Fig. 2) showed it to be a structure intimately associated with a normal gallbladder. An upper gastrointestinal examination performed shortly thereafter demonstrated the presence of a very large duodenal bulb which undoubtedly accounted for the mass visualized on the routine abdominal roentgenogram. The enlargement of the bulb was due to a rather voluminous, irregularly outlined intraluminal soft tissue mass, which appeared to have a central ulceration (Fig. 3). The bulb was freely movable and compressable, and no tenderness could be elicited. The barium flowed freely around the mass into the distal duodenum. No erosion of the duodenal mucosa could be demonstrated on multiple spot roentgenograms of the area. The roentgenographic appearance of the lesion was quite reminiscent of the large benign tumors sometimes encountered in the stomach. Because of this similarity and because of the soft and unobstructive nature of this rather large lesion, the diagnosis of benign tumor of the duodenal bulb was offered preoperatively.

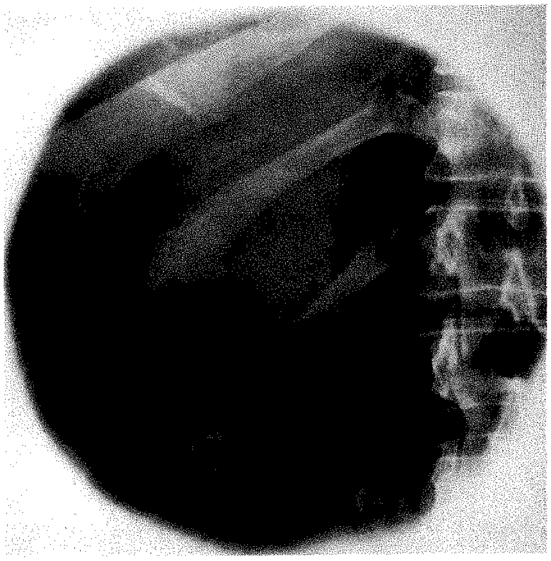


Fig. 1. "Coned down" view of the mass in the right upper quadrant of the abdomen.

On October 10, laparotomy was performed with duodenotomy which revealed a 4×5×9 cm. pedunculated polypoid mass in the duodenal bulb (Fig. 4, *A* and *B*). A portion of the

---

* From USA Tripler General Hospital.

This material has been reviewed by the Office of the Surgeon General, Department of the Army, and there is no objection to its presentation and/or publication. This review does not imply any endorsement of the opinions advanced or any recommendations of such products as may be named.

† Radiology Service.

‡ Department of Surgery. Now at De Witt Army Hospital, Ft. Belvoir, Va.

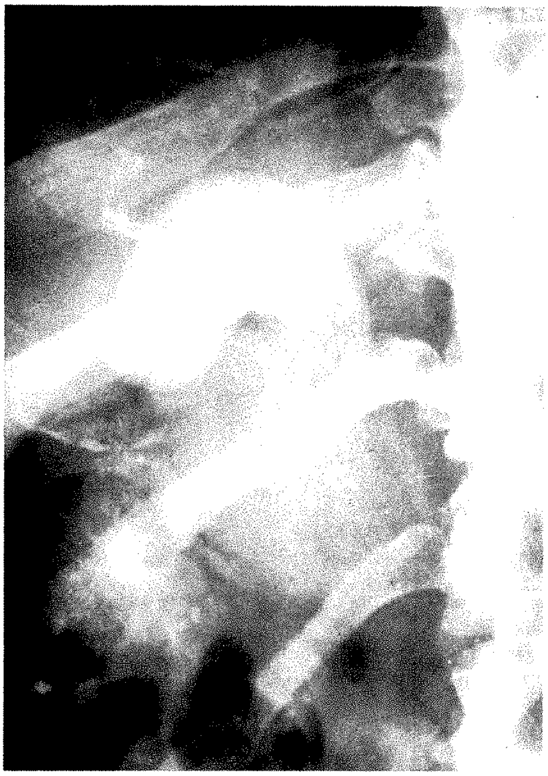


FIG. 2. Oral cholecystogram. The gallbladder is "draped" over the mass.

soft mass had passed through the pylorus into the stomach. The lesion originated on a rather short stalk whose base was situated a few millimeters distal to the pyloric ring. The lesion was removed in continuity with the neighboring portion of the stomach and duodenum and at surgery it appeared grossly to be an adenoma. There was no evidence of ulceration. Histologic sections of the lesion were interpreted as papillary adenoma of the duodenum.

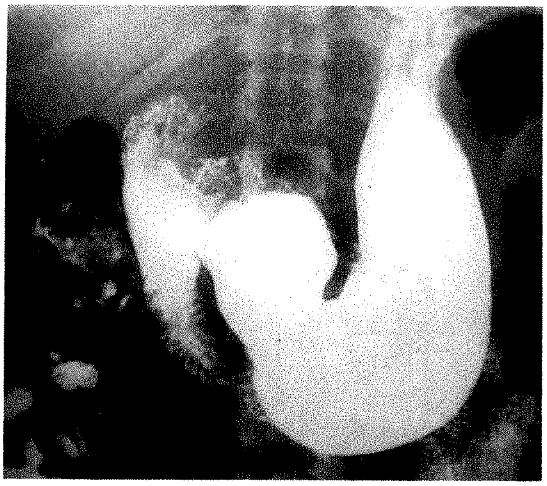


FIG. 3. Upper gastrointestinal examination showing the enlarged duodenal bulb and its extremely irregular filling defect. The small collection of barium in the center of the defect suggested ulceration. The enlarged bulb corresponds in location to the soft tissue mass previously demonstrated.

DISCUSSION

The incidence of benign tumors of the duodemun is probably best documented by Raiford[6] who found 21 duodenal tumors in 11,500 autopsies and 45,000 surgical specimens at the Johns Hopkins Hospital, 13 of

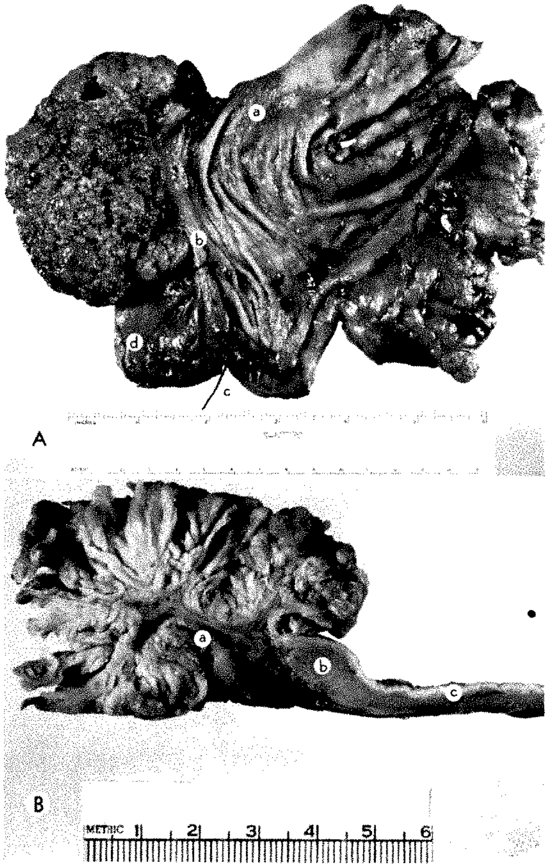


FIG. 4. The surgical specimen. (*A*) The polypoid mass is located just distal to the pyloric ring (indicated by the suture). (a) Stomach, (b) pylorus, (c) string on pylorus, (d) duodenum. (*B*) Longitudinal section through the specimen shows the stalk arising from the duodenum immediately distal to the pylorus. (a) Stalk, (b) pylorus, (c) gastric mucosa.

which were benign. Until 1957 there were 201 benign tumors of the duodenum reported in the literature.[4] Cole[3] reviewed a series of 90 benign duodenal tumors and found that adenomas constituted 42.2 per cent and fibromyomas 18.8 per cent of the total.

The clinical history in patients with these lesions is quite unimpressive in spite of the relatively large size these tumors can attain. Benign tumors of the small bowel, in general, vary in size from that of a grain of wheat to that of a fetal head.[7] Most of these tumors are intrinsic and extend toward the bowel lumen,[2] and, although it would seem that obstruction should occur when they reach the size of the intestinal lumen, such is not usually the case. When symptoms do occur, hemorrhage is the predominant presenting feature. Occasionally, there may be some vague upper abdominal distress such as might occur with duodenal ulcer.[1]

Because of the relatively asymptomatic nature of these lesions and because of their usually small size, they are not frequently diagnosed roentgenographically. Occasionally, as in our case, the roentgenographic picture is quite striking. We believe that this is the first time a benign tumor of the duodenal bulb has been shown to produce a shadow on a routine roentgenogram of the abdomen. Moersch *et al.*[5] have recently reported a case of villous adenoma of the duodenum in a 67 year old female who complained only of vague epigastric distress. A representative roentgenogram from a barium study was included in the report and its similarity to the roentgenograms in our case is remarkable.

SUMMARY

A case of a large adenoma of the duodenal bulb is reported not so much because of its rarity but because it produced roentgenographic signs on both, routine and contrast studies. A brief discussion of the incidence of benign duodenal tumors and their clinical findings is presented to account for their infrequent demonstration by roentgenographic techniques.

Carl W. Boyer, Jr., Major, MC, USA
Radiology Service
U. S. Army Tripler General Hospital
APO 438
San Francisco, California

REFERENCES

1. Balfour, D. C., and Henderson, E. F. Benign tumors of duodenum. *Ann. Surg.*, 1929, *89*, 30–35.
2. Briggs, J. D., and Roberts, J. F. Gastrointestinal hemorrhage from benign tumors of duodenum. *A.M.A. Arch. Surg.*, 1953, *66*, 10–19.
3. Cole, D. R. Fibromyoma of duodenum. *A.M.A. Arch. Surg.*, 1953, *66*, 392–396.
4. Culver, G. J., and Caccese, R. Benign intraluminal polypoid adenoma of first portion of duodenom. *Radiology*, 1957, *69*, 263–265.
5. Moersch, R. N., Woolner, L. B., and Clagett, O. T. Villous adenoma of duodenum. *Surgery*, 1962, *51*, 574–577.
6. Raiford, T. S. Tumors of small intestine. *A.M.A. Arch. Surg.*, 1932, *25*, 122–177; and 321–355.
7. River, L., Silverstein, J., and Tope, J. W. Benign neoplasms of small intestine. *Surg., Gynec. & Obst.* (*Int. Abst. Surg.*), 1956, *102*, 1–38.

INTRALUMINAL DUODENAL DIVERTICULUM

By J. C. H. LAUDAN, M.D.,* *and* G. I. NORTON, M.D.†
VANCOUVER, B. C., CANADA

INTRALUMINAL diverticulum of the duodenum occurs rarely, but to date at least 12 case reports of this abnormality can be found in the medical literature. In these reports, the characteristic and rather startling roentgenographic appearance of this seemingly self-contradictory diverticulum is well described. Typically, on barium examination, a barium-filled sac appears within the duodenal lumen, arising near the papilla of Vater and never extending beyond the confines of the duodenal lumen in any projection. On pressure spot roentgenograms particularly, a thin radiolucent halo is seen to outline and to represent the wall of the diverticulum. A degree of dilatation of the duodenum proximal to the sac may be present. Concretions or foreign bodies within the sac[17] and related or unrelated anatomic abnormalities have been observed. The presence of the latter in the form of aberrant or annular pancreas,[2] anomalous entrance of the bile and pancreatic ducts,[6] or additional duodenal septa, is of obvious surgical importance, particularly since the ostium of the intraluminal diverticulum is, as noted above, usually at or near the level of the papilla of Vater. The papilla can be, and has been, damaged at surgery.[5]

REPORT OF A CASE

Mrs. E.C., a 26 year old white woman, had a barium meal examination because of a 5 day episode of epigastric distress relieved by food. There was no history of obstructive symptoms or of gastrointestinal bleeding.

On the study a duodenal ulcer, measuring 1 cm. in diameter, was clearly demonstrated in the anterior wall of the duodenal bulb, as well as an intraluminal diverticulum arising from the second part of the duodenum near the ampulla of Vater (Fig. 1). This diverticulum was about 10 cm. long and extended distally into the third part of the duodenum. It appeared to fill and empty, and to change its size and shape (Fig. 2–5). When the diverticulum was empty, its wall could still be identified as a radiolucent streak in the second and third part of the duodenum (Fig. 2) somewhat simulating the appearance of a tapeworm. The proximal ostium of the diverticulum appeared to measure about 1 cm. in diameter. The ease with which the sac emptied suggested the presence of a distal ostium, as well.

The patient was placed on medical treatment with prompt relief of symptoms and, to date, there has been no indication for surgery. (Case presented with the kind permission of Dr. Leo Friesen, Vancouver, B. C.)

REVIEW OF THE LITERATURE

In cases discovered by barium studies of the upper gastrointestinal tract, the

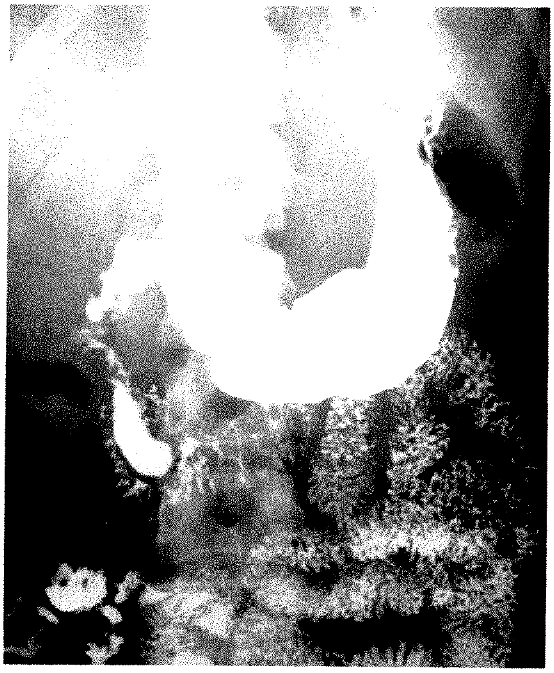


FIG. 1. Diverticulum filled and ulcer crater in bulb.

---

* Senior Intern in Radiology, Shaughnessy Hospital, Department of Veterans Affairs, Vancouver, B. C., Canada.

† Consultant Radiologist, Radiological Services, Shaughnessy Hospital, Department of Veterans Affairs, Vancouver, B. C., Canada.

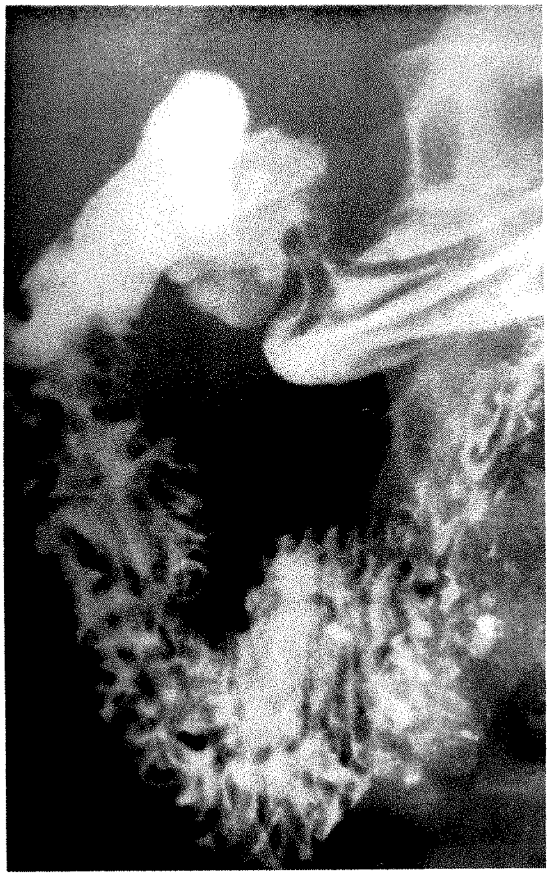


Fig. 2. Diverticulum empty with its wall showing as radiolucent streak.

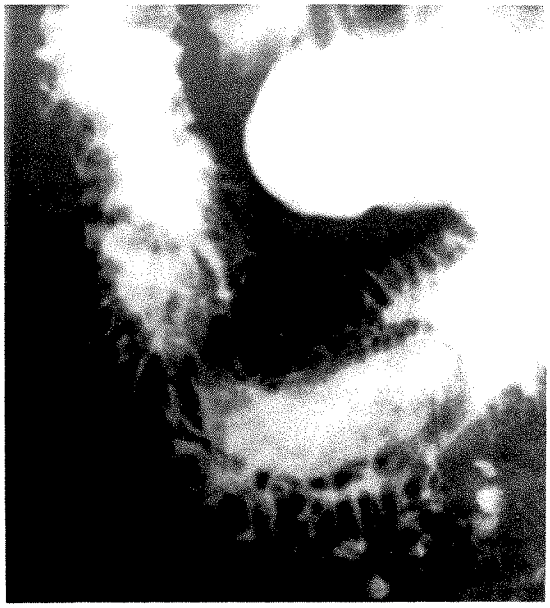


Fig. 3. Diverticulum partially filled.

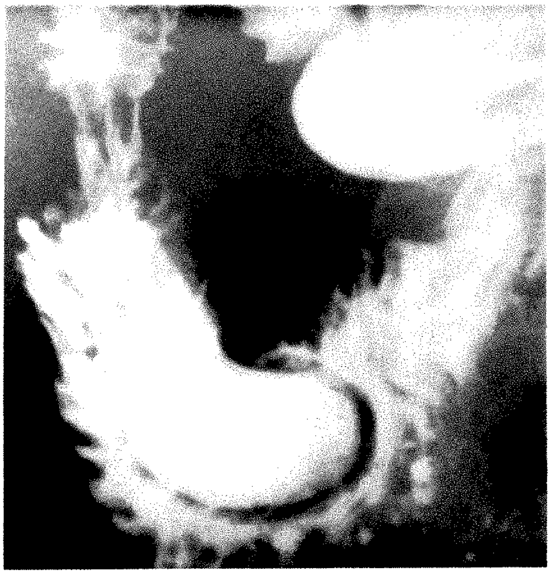


Fig. 4. Diverticulum fully filled showing "halo" sign.

examination had been performed to determine the cause of rather nonspecific symptoms suggesting partial obstruction, peptic ulcer, or gastrointestinal bleeding. Peptic ulcer has, in fact, been found in 3 cases including the present case, and in one of these[23] a bleeding ulcer was found to lie

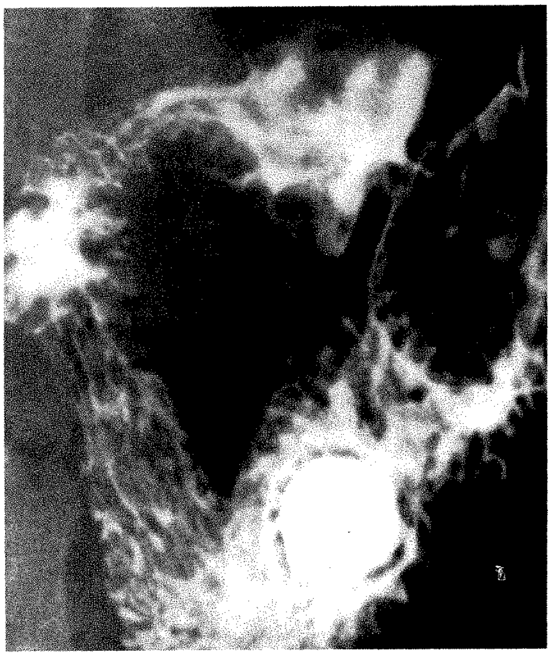


Fig. 5. Diverticulum changing its shape and size.

within the diverticulum itself, just distal to its ostium.

It is of interest to note that in 3 cases[6,14,18] previous roentgenographic examination had not disclosed the diverticulum as such, presumably because of its failure to fill.

These diverticula are thought to arise as a result of incomplete recanalization of the duodenum following the normal luminal obliteration stage of the embryonic gut. This recanalization occurs as a coalescence of vacuoles, and so it seems reasonable that

Table I

CASES OF INTRALUMINAL DUODENAL DIVERTICULUM REPORTED IN THE LITERATURE

	Sex	Age	Symptoms	Roentgen Findings	Operative Findings
Nelson[18] 1947	Female	27	Right upper quadrant pain	At least 3 stomach and duodenum examinations before diagnosis made; typical halo, proximal dilatation of duodenum	Circumferentially attached diaphragm with 1 cm. aperture laterally and pouch (diverticular) ostium medially below papilla Vateri which opened on posterior duodenal wall
Kinzer[13] 1949	Male	22	Acute abdominal pain, partial obstruction	Typical "gourd" surrounded with lucent halo in 2nd part, megabulbus	Simple sac with mucosa on both surfaces, ostium just distal to ampulla
Meyer and Edgren[17] 1956	Female	33	Intermittent mild obstruction, symptoms since childhood	Typical, megaduodenum	Circumferentially attached large sac with 5 mm. distal opening, containing corroded penny (swallowed in childhood), dilated duodenum proximally to attachment just below ampulla
Zatzkin, Macy and Kveton[23] 1959	Male	40	Gastrointestinal bleeding, ulcer-like pain for months	Typical, ulcer not seen	4×8 cm. pouch with 1 cm. attachment to duodenal wall opposite ampulla with bleeding ulcer crater in the sac wall just distal to its attachment, pancreatic duct also opened opposite the ampulla in the same plane as the sac attachment
Köhler[14] 1960	Female	33	Eructation, intermittent epigastric pain for 5 years, healed gastric ulcer diagnosed 3 years previously	Typical, some proximal duodenal dilatation	3×8 cm. sac with a stoma 2/3 duodenal circumference containing some concretions, ampulla distal to the sac ostium
Coors and Mitchum[6] 1962	Male	23	Epigastric bloating, burning, nausea	Typical, but no dilatation of proximal duodenum	4.2×2.3 cm. sac with 1.2 cm. orifice arising from lateral mucosal fold of the ampulla, anterior subserosal aberrant pancreatic tissue connected to head of pancreas at level of ampulla, no ulcer
Buisseret and Van Den Eynde[5] 1962	Female	35	Intestinal obstruction	Typical, proximal dilatation of duodenum	Large sac with ostium arising from duodenal bulb posteriorly 1 cm. from pylorus, megaduodenum, malrotation of duodenum, complicated by acute pancreatitis postoperatively
Hirsch and Mal[10] 1962	Male	56	Vague epigastric distress	Large, typical, arising high in second part of duodenum, being drawn down into the third part of a long redundant duodenum	Not operated on
Wiot and Spiro[22] 1963	Male	47	Disappearing epigastric "lump" postprandially, with nausea	Typical	6 cm. sac arising from the medial wall near the papilla Vateri
	Male	57	Vague gastrointestinal symptoms for 1 week	Typical	Not operated on
Laudan and Norton 1963	Female	26	Epigastric distress for 5 days	Typical	Not operated on

a blind pouch, a tube, a cyst, or a diaphragm could arise from a failure of complete reconstitution of a single-lumen duodenum. In fact, all varieties of anomaly one could reasonably expect from this mechanism have been described. Two major theories of origin of the intraluminal diverticulum have been proposed to explain the details of its development.

The intraluminal diverticulum can be considered to have developed as such by relative isolation of an embyronic vacuole which had a communication with the main duodenal lumen. It would, in this case, represent a somewhat incomplete variety of duodenal duplication, a more complete form of which is represented by the enterogenous cyst.[3,22] Enterogenous cysts are, however, fairly rare in the duodenal area,[8,15] at least on comparison with duodenal diaphragms, which are invoked as the raw material for the second major hypothesis of the origin of the intraluminal diverticulum. Although duodenal diaphragms are found in adults as unaltered flat projections into the lumen,[11,18,20] this variety apparently neither occludes the lumen enough to build up back-pressure, nor is sufficiently thin to become distended by such pressure as is developed. The type of duodenal diaphragm from which intraluminal diverticula develop are fairly obviously those which for functional anatomic reasons can become ballooned out. The classic situation is that of the circumferential attachment with a distal hole in the sac to re-establish continuity with the gut lumen.[2,17,19] Nelson,[18] who reported what is probably the first roentgenologic demonstration of intraluminal duodenal diverticulum, reviewed the literature on the subject of intraduodenal diaphragms, collecting 35 cases reported between 1845 and 1944, and considered his case to be one of a redundant duodenal diaphragm, not making a point of the diverticular-like transformation. Nevertheless, his case is now considered to demonstrate an intraluminal diverticulum, as, in fact, would some of those cases he reviewed, had they been subjected to appropriate investigation prior to operation or autopsy.

Whether the intraluminal diverticula develop from diaphragm or duplication or whether they might also arise from a budding-off of undifferentiated entodermal cells in the early embryo,[15] all cases so far reported present surprisingly similar roentgenographic appearances (Table I).

Consideration of the surgical removal of an intraluminal duodenal diverticulum would seem to be tempered by the presence or absence of obstruction, or of peptic ulcer, and by the general surgical risk together with the added risk of the possible presence of other regional anatomic abnormalities, rather than to be based upon the finding of the intraluminal diverticulum *per se*.[10,22]

SUMMARY

A case of intraluminal diverticulum of the duodenum, with a coexisting duodenal ulcer is reported. The relevant literature has been reviewed and the etiology of the abnormality briefly discussed.

J. C. H. Laudan, M.D.
Radiological Service
Shaughnessy Hospital
Vancouver 9, B. C., Canada

REFERENCES

1. Baroody, W. G., Innes, R., and Harrison, H. N. Enterogenous cyst of duodenum. *Gastroenterology*, 1956, *30*, 523–528.
2. Bill, A. H., Jr., and Pope, W. M. Congenital duodenal diaphragm: report of two cases. *Surgery*, 1954, *35*, 482–486.
3. Bremer, J. L. Diverticula and duplications of intestinal tract. *Arch. Path.*, 1944, *38*, 132–140.
4. Broker, H. M., and Hay, L. J. Case report of two spherical duplications of second portion of duodenum in 54 year old patient. *Surgery*, 1955, *37*, 996–1001.
5. Buisseret, E., and Van Den Eynde, P. Un type particulier de diverticule duodénale. *Acta gastro-enterol. belg.*, 1962, *25*, 129–132.
6. Coors, G. A., and Mitchum, W. R. Intraluminal duodenal diverticulum. *Am. J. Surg.*, 1962, *103*, 400–402.
7. Drucker, V., and Cohen, E. S. Megaduodenum secondary to intrinsic duodenal diaphragm. Am. J. Roentgenol. & Rad. Therapy, 1946, *55*, 726–729.
8. Faegenburg, D., and Bosniak, M. Duodenal

anomalies in adult. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *88*, 642–657.

9. Flachs, K. Incomplete congenital septa of duodenal bulb. *Acta radiol.*, 1962, *57*, 237–240.
10. Hirsch, F., and Mal, R. À propos d'un cas de diverticule intraduodénal. *Acta gastro-enterol. belg.*, 1962, *25*, 139–141.
11. Hudson, C. N. Congenital diaphragm of duodenum causing intestinal obstruction in adult. *Brit. J. Surg.*, 1961, *49*, 234–236.
12. Jelenko, C. Duplication of duodenum: review and report of case. *Am. Surgeon*, 1962, *28*, 120–132.
13. Kinzer, R. E. Intraluminal diverticulum and other lesions producing intermittent duodenal obstruction or stasis. Am. J. Roentgenol. & Rad. Therapy, 1949, *61*, 212–218.
14. Köhler, R. Intraluminal duodenal diverticulum: report of case. *Acta radiol.*, 1960, *54*, 439–442.
15. Ladd, W. E., and Gross, R. E. Surgical treatment of duplications of alimentary tract: enterogenous cysts, enteric cysts and ileum duplex. *Surg., Gynec. & Obst.*, 1940, *70*, 295–307.
16. Mendl, K., and Sharp, M. E. Redundant duodenal mucosal folds and retrograde prolapse through pylorus. *Brit. J. Radiol.*, 1960, *33*, 36–42.
17. Meyer, A. C., and Edgren, D. C. Duodenal obstruction by intraluminal diverticulum. *A.M.A. Arch. Surg.*, 1956, *73*, 1058–1059.
18. Nelson, W. I. Congenital diaphragm of duodenum: case report with preoperative x-ray studies. *Minnesota Med.*, 1947, *30*, 745–752.
19. Pearson, C. C. Unusual causes of duodenal deformity as seen roentgenographically. *Gastroenterology*, 1956, *30*, 447–461.
20. Saunders, J. B. de C. M., and Lindner, H. H. Congenital anomalies of duodenum. *Ann. Surg.*, 1940, *112*, 321–338.
21. Turunen, M. Intraluminal duodenal diverticulum: report of case. *Acta chir. scandinav.*, 1961, *122*, 535–538.
22. Wiot, J. F., and Spiro, E. Intraluminal diverticulum: form of duplication. *Radiology*, 1963, *80*, 46–49.
23. Zatzkin, H. R., Macy, J. J., and Kveton, F. W. Intraluminal duodenal diverticulum: report of case. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *82*, 1036–1037.

* * *

ACUTE ORGANO-AXIAL GASTRIC VOLVULUS

By LEO S. FIGIEL, M.D., *and* STEVEN J. FIGIEL, M. D.
DETROIT, MICHIGAN

ACUTE organo-axial gastric volvulus occurs rarely. Early recognition of this entity is of paramount importance since death may result from strangulation of the viscus in a matter of hours. Although clinically the findings are frequently characteristic, roentgenographically they are usually pathognomonic. Immediate surgical intervention is indicated when this condition is known to exist.

In most cases of acute organo-axial gastric volvulus, the greater curvature of the stomach swings forward and upward causing the whole stomach to revolve on its long axis. In other words, the gastric cardia becomes dependent and the pyloric portion of the stomach becomes superior-most and lies beneath the diaphragm. Obstruction results at both extremities of the stomach, that is, at the esophagogastric junction and in the pyloric portion and is undoubtedly the result of twisting or volvulus at the two extremities of the stomach.

In the acute form, as distinguished from displacement and/or rotation seen with eventration of the diaphragm, phrenic crush, or with herniation of the entire stomach through the esophageal hiatus, usually manifestations of the classic clinical triad of Borchardt and Lenormant will be noted.[5] Patients afflicted with acute organo-axial gastric volvulus complain of sudden onset of circumscribed severe epigastric pain, of vigorous efforts to vomit without results, and the physician will note an inability to pass a stomach tube or to successfully aspirate an obviously distended stomach. Shock may develop early in the course of the disease. These symptoms should alert the clinician to the possible presence of acute gastric volvulus.

Ordinarily, aspiration of large amounts of fluid and gas by means of a tube with clinical findings indicating decompression of the stomach as evidenced by decreased distention and decreased tympany in the left upper abdomen should rule against gastric volvulus; however, occasionally, a tube will enter the stomach in the acute form of volvulus and considerable gas and fluid may be aspirated (Case II). It is obvious then, that an accurate diagnosis must be made by other means. In our experience acute organo-axial gastric volvulus presents characteristic findings on scout roentgenograms of the abdomen, permitting an accurate and reliable diagnosis early in the course of this disease.

ROENTGEN FINDINGS

Roentgenographically, in these cases the gastric cardia is markedly dilated or distended and presents in the left upper and mid-abdomen, frequently extending across the midline into the right abdomen. The contour of the gastric cardia which is convex on all surfaces will readily permit identification and differentiation from the usual forms of gastric obstruction or dilatation in which the stomach preserves a normal appearance of its curvatures, *i.e.*, the lesser curvature of the stomach in obstruction or acute dilatation remains concave. A long fluid level will be seen extending across the cardia.

Distention of the pyloric end of the stomach is much less marked and may be relatively inconspicuous. Tbe pyloric portion lies beneath the diaphragm above the distended cardia. An upright study usually shows a much smaller fluid level more superiorly in this segment of the stomach, generally medially in the left upper quadrant; however, it may extend across the midline to the right. The diaphragmatic leaf on the left may be elevated due to a marked distention of the stomach but this finding may be seen in cases of acute gastric dilatation or gastric obstruction and as such is not necessarily of diagnostic importance.

If a tube or catheter has been introduced into the esophagus, fluoroscopically or on roentgenographic study, it may coil upon itself in the lower esophagus. The bolus of the coiled tubing in some instances will indicate the approximate diameter of the esophagus, which if dilated will, of course, suggest obstruction. Coiling of the tube in the lower esophagus in conjunction with the described findings on a scout study of the abdomen indicates obstruction at the esophagogastric junction presumptively due to volvulus.

Contrast studies after administration of a small quantity of opaque material, dilute barium or water soluble iodine compounds should demonstrate high-grade or complete obstruction at the esophagogastric junction. Distortion or twisting of the mucosal folds at the point of obstruction, occasionally with a beak-like appearance, is conclusive evidence for a diagnosis of gastric volvulus.

REPORT OF CASES

Case I. (Fig. 1, *A–E*). E. W., a 69 year old Negro male, was admitted on March 5, 1961 because of complaints of nausea, vomiting and abdominal pain. The patient had been in excellent health until approximately 24 hours prior to admission at which time he began to vomit all ingested food. The vomitus consisted of undigested food at the onset with progression to nonproductive retching. Enlargement of the abdomen and abdominal pain were noted later. The pain was generalized and was not relieved by vomiting or changes in position of the patient.

Physical examination on admission revealed a thin male who was alert, cooperative and well oriented. The blood pressure was 100/70. The pulse rate was 92 per minute and weak. The upper abdomen was markedly distended and an area of increased tympany was noted in the gas-

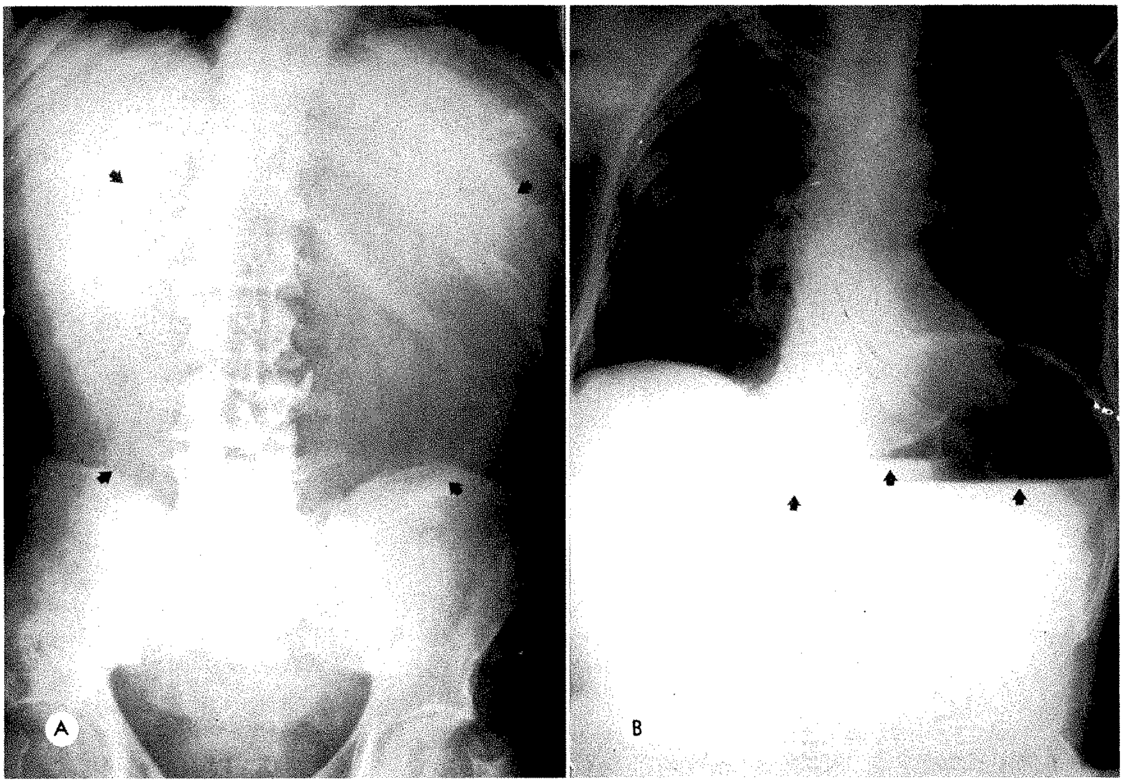


Fig. 1. Case I. (*A*) Roentgenogram showing the markedly distended viscus in the upper abdomen (arrows). The margins of this viscus are convex on all surfaces. (*B*) Large fluid level is seen in the cardia (lower arrows). Shorter fluid level is seen more superiorly (upper arrow) in the pyloric portion of stomach.

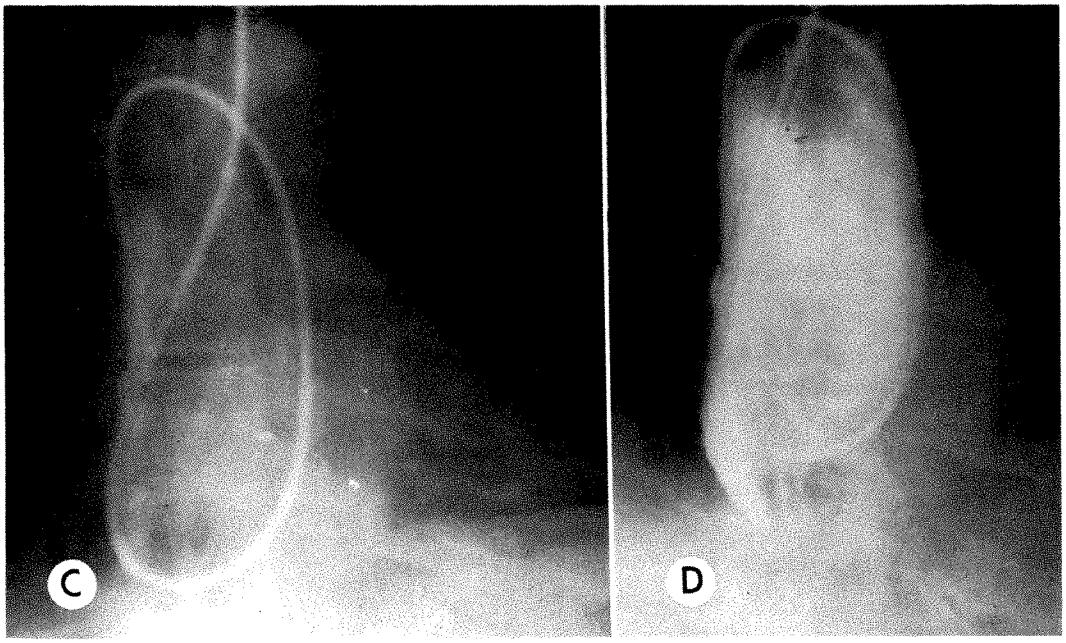


FIG. 1. (*C*) Coiling of the catheter is seen in the esophagus with dilatation of the esophagus. (*D*) Contrast study showing complete block at the esophagogastric junction. Note the pointed or beak-like appearance at the site of the obstruction.

tric region. There was also a marked degree of spasm and tenderness in the mid and upper abdomen.

Roentgenographic studies of the abdomen showed a large distended viscus in the left upper abdomen. On this basis a Levine tube was inserted, connected to continuous suction, and intravenous fluids were begun.

It was noted shortly that Levine tube drainage had stopped without any change occurring in the size of the abdomen. Approximately 200 cc. of dark brown fluid had been removed. Irrigation of the Levine tube proved it to be patent but return of gastric content did not occur. Efforts to pass a Cantor tube were unsuccessful and no drainage of gastric contents was noted. At this time the blood pressure dropped to 80/20 mm. Hg with a rise of the pulse rate to 120–140 per minute. Nasal oxygen and blood were given. It was also noted that there was an increase in abdominal pain and an absence of bowel sounds. The patient remained in shock despite the above measures. Clinically at this time it was felt that he had acute pancreatitis, but perforation and mesenteric thrombosis could not be ruled out. Supportive measures were continued.

Repeat anteroposterior and upright studies of the abdomen were obtained and the roentgenologic impression was that of acute organo-axial gastric volvulus. Fluoroscopic studies of the chest revealed an opaque catheter coiled upon itself in the lower esophagus, its bolus indicating dilatation of the esophagus. Gastrografin was injected and a dilated esophagus was demonstrated. There was a pointed termination to the esophagus at the esophagogastric junc-

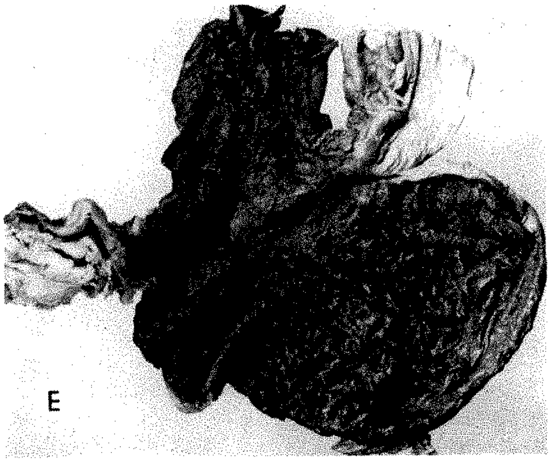


FIG. 1. (*E*) Pathologic specimen showing abrupt termination of normal and gangrenous portion at the esophageal and pyloric extremities of the stomach.

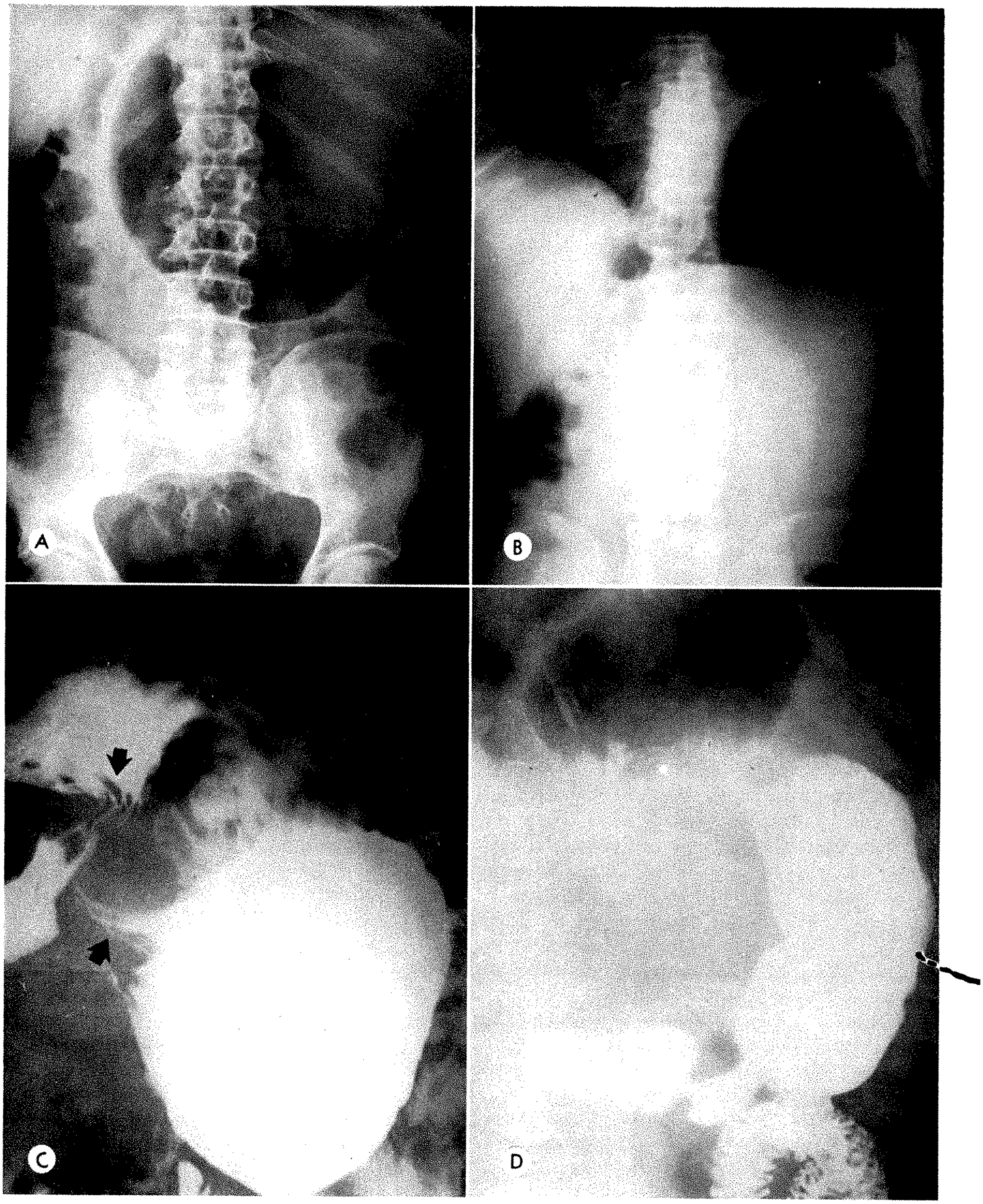


Fig. 2. Case II. (*A*) Roentgenogram showing the markedly distended stomach with convex borders. (*B*) Two fluid levels are seen, the larger in the gastric cardia and the smaller fluid level is seen more superiorly and medial to the spine in the pyloric end of the somach. (*C*) Roentgenogram demonstrating organo-axial orientation of the stomach. Twisting of mucosa is suggested at both extremities of the stomach (arrows). (*D*) Roentgenogram made in 1951 showing normal orientation of this patient's stomach.

tion, suggesting twisting or volvulus at this site.

Surgical consultation was obtained and it was felt that, in spite of the patient's poor condition, laparotomy and gastrostomy were advisable.

Under local anesthesia the abdomen was opened and marked distention was encountered in the upper abdomen. The gastric wall was very thin and bluish in appearance. A small incision was made in the stomach and, under pressure, approximately 3,000 cc. of black watery liquid was removed. A Foley catheter was placed in the gastrostomy and a 30 cc. bag inflated. The patient remained in a poor condition following surgery and died on March 7, 1961, less than 27 hours following admission.

At autopsy, the stomach was found to be rotated along the longitudinal cardiopyloric axis from left to right and from below upward. The anterior surface of the stomach faced posteriorly while the posterior surface was on the abdominal wall and was veiled by the gastrocolic omentum. The cardia of the stomach was thus dependent in position. The pylorus and first portion of the duodenum appeared to be abnormally mobile and displaced to the left. The stomach was dilated and measured about 35 cm. in length along the greater curvature and 18 cm. in lentgh along the lesser curvature. The mucosa at the cardia and pyloric ring was pale red in color; otherwise, the remainder of the entire wall of the stomach was blue-black, thin and pliable. The mucosal folds were completely effaced and no ulcer or new growth was present. The position of the transverse colon was below the level of the rotated stomach.

Case ii. (Fig. 2, *A–D*). J. F., a 68 year old white male, presented with a chief complaint on admission of a severe attack of epigastric pain associated with nausea and retching but no vomiting. He stated that during the previous 4 or 5 years he had had recurrent attacks of epigastric pain following a large meal which lasted from 3 to 5 days. The distress was constant in character and described as fullness with retching but never any vomiting or belching. During these attacks he could only consume small quantities of fluid. In his opinion the present attack was the most severe of all.

Physical examination revealed marked tympany in the region of the stomach suggesting gastric enlargement.

Roentgenographic studies of the abdomen were obtained on August 30, 1954 and were interpreted as a probable pyloric obstruction. Repeat scout studies demonstrated no change in the appearance of the stomach.

During his stay in the hospital, a Levine tube was passed and connected to suction. Between August 31, 1954 and September 3, 1954 approximately 4,000 cc. of reddish brown to light purple fluid was removed from the stomach. An upper gastrointestinal study on September 4, 1954 revealed an organo-axial orientation of the stomach with twisting noted at the esophagogastric junction and in the pyloric portion of the stomach. The diameter of the stomach had decreased markedly in the interim.

Surgical intervention on September 10, 1954 showed considerable dilatation of the stomach; however, no organic lesion of any type was discovered. No definitive procedure was carried out. The patient recovered and was discharged.

SUMMARY

1. Acute gastric volvulus should be suspected clinically when a patient presents with acute upper abdominal pain and unsuccessful efforts to vomit, especially when there is inability to pass a long tube or inability to decompress an obviously distended stomach.

2. The combination of a markedly distended viscus in the left upper and mid abdomen which has a smooth convex border and the demonstration of two fluid levels should be considered diagnostic of acute organo-axial gastric volvulus.

3. Coiling of a tube or catheter in the lower esophagus when associated with these findings is indicative of obstruction due to gastric volvulus.

4. Contrast studies will usually show complete obstruction and may demonstrate a beak-like appearance characteristic of volvulus.

5. Surgical intervention is immediately indicated in acute gastric volvulus.

Leo S. Figiel, M.D.
1429 David Whitney Building
Detroit 26, Michigan

THE "RING" SHADOW IN THE DIAGNOSIS OF ULCER*

By MORTIMER LUBERT, M.D., *and* GEORGE R. KRAUSE, M.D.
CLEVELAND, OHIO

IT IS our purpose to examine the circumstances under which ulcers of the stomach and duodenum appear as "rings" and to point out how this information may be put to use in contrast examinations of the upper gastrointestinal tract.

DIAGNOSTIC POSSIBILITIES OF RING SHADOWS

Templeton[4] did describe "ring craters" and Meuwissen[2] elaborated on "frontal" ulcers. Neither, however, fully exploited the diagnostic possibilities of this sign of ulcer. This is understandable since they were emphasizing mucosal studies and compression techniques. With small quantities of barium sulfate, an ulcer may appear as a ring because of incomplete filling. This is a transient phenomenon. With further filling, the ring is replaced by the "fleck." Pressure at this time will reveal a ring only if there is a filling defect at the base (Fig. 1). Despite the rarity of this occurrence, it has been the point of major emphasis.

With the increasing use of double contrast studies popularized by Hampton[1] for the duodenal cap and by Schatzki and Gary[3] for the upper portion of the stomach, visualization of an ulcer as a ring will occur more often. The ulcer need not have a filling defect in its depth and the ring will be of considerable usefulness in the diagnosis of ulcer.

In double contrast studies, ulcers may appear as rings depending on their position, wall configuration and barium content. When the patient is supine, ulcers on the anterior wall almost invariably appear as rings (Fig. 2; 3, *A* and *B;* and 4, *A* and *B*). However, ulcers elsewhere may also appear

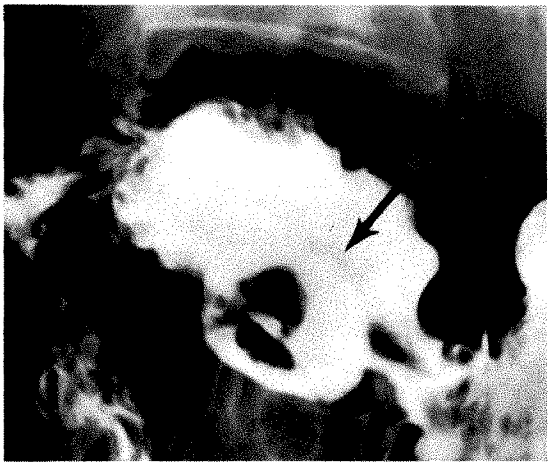


Fig. 1. Compression spot roentgenogram of bulb demonstrating crater with filling defect in base (arrow). Pancreatic tissue at operation.

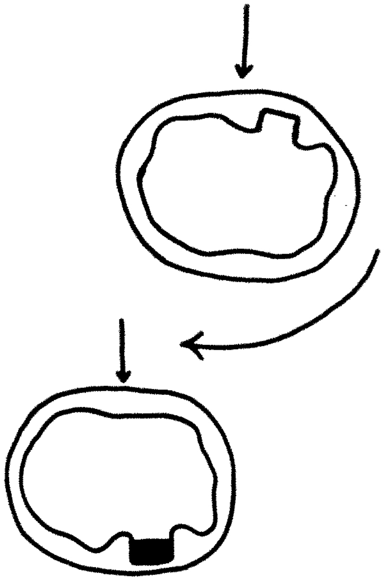


Fig. 2. Diagram representing appearance of a crater as a "ring" or as a barium niche. The ulcer appears as a ring when it is superior and as a barium-filled fleck when it is dependent.

---

* From the Department of Radiology, Mount Sinai Hospital of Cleveland, Ohio.
Presented in exhibit form at the Sixty-third Annual Meeting of The American Roentgen Ray Society, Washington, D. C., October 2–5, 1962.

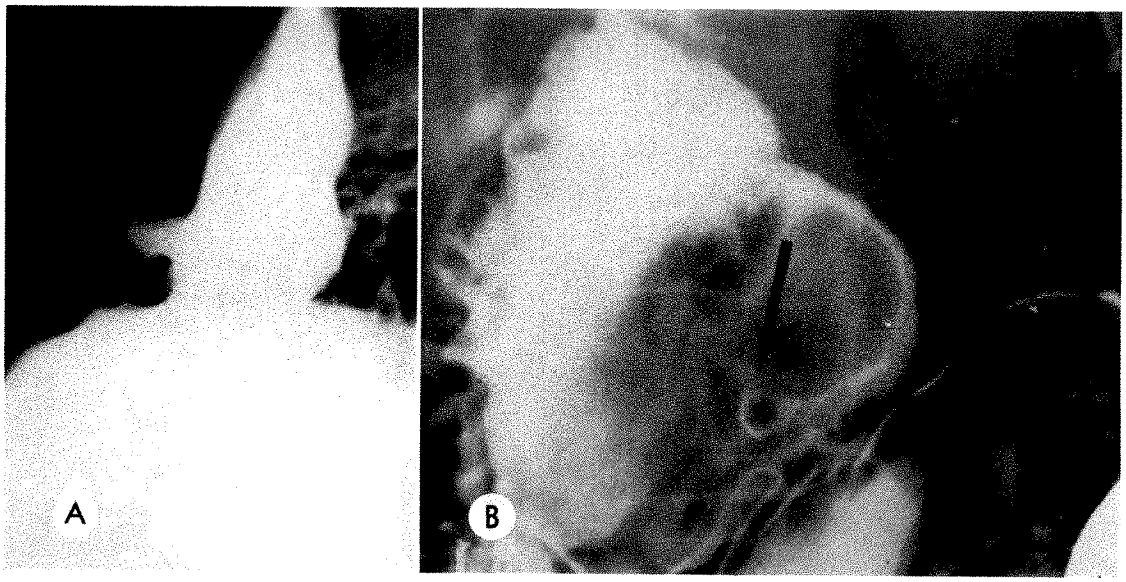


Fig. 3. (*A*) Anterior wall duodenal niche in second oblique position. No filling defect in base. (*B*) Double contrast study with patient supine shows the anterior ulcer as a ring (arrow).

as rings if they are in an inverted position during observation or if they have lost their barium content during manipulation and have not been refilled (Fig. 5, *A* and *B*). In addition to being barium-impregnated, the ulcer wall must be tangential to the central ray in order to appear as a ring. If only part of the wall is so situated, only a partial ring will be seen (Fig. 6, *A* and *B*).

The most frequent application of the ring will be to confirm an ulcer already seen on the conventional roentgenogram (Fig 3, *A* and *B;* and 7, *A* and *B*). Not only will this add substance to the original observation but also may provide information about the location of the crater when rotation is confusing or impossible (Fig. 8, *A* and *B*). Rarely, the ring may be the first or only

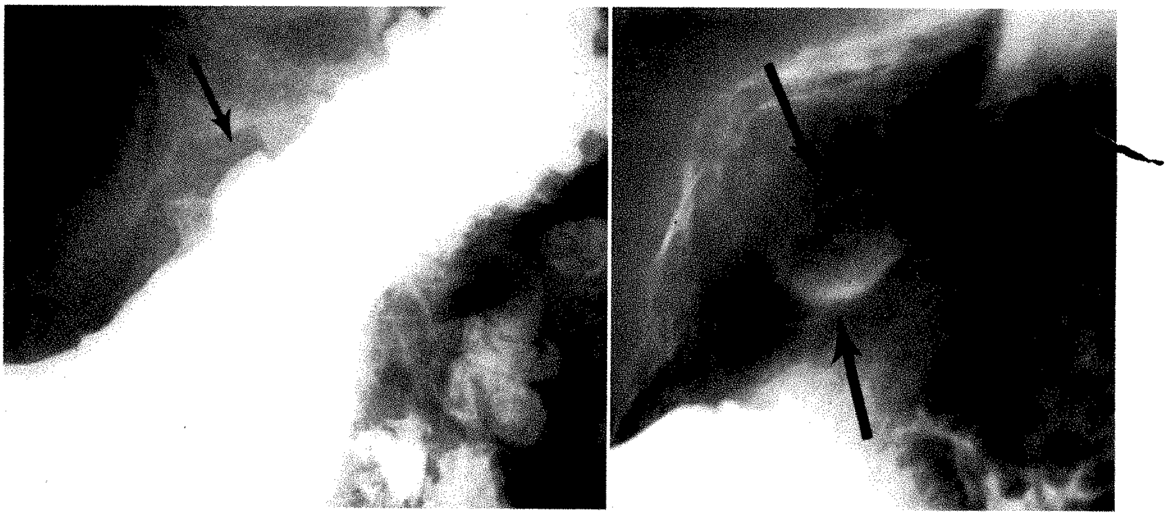


Fig. 4. (*A*) Questionable crater on irregular anterior gastric wall (arrow). (*B*) Ring (arrows) proves the presence of ulcer in gas distended stomach.

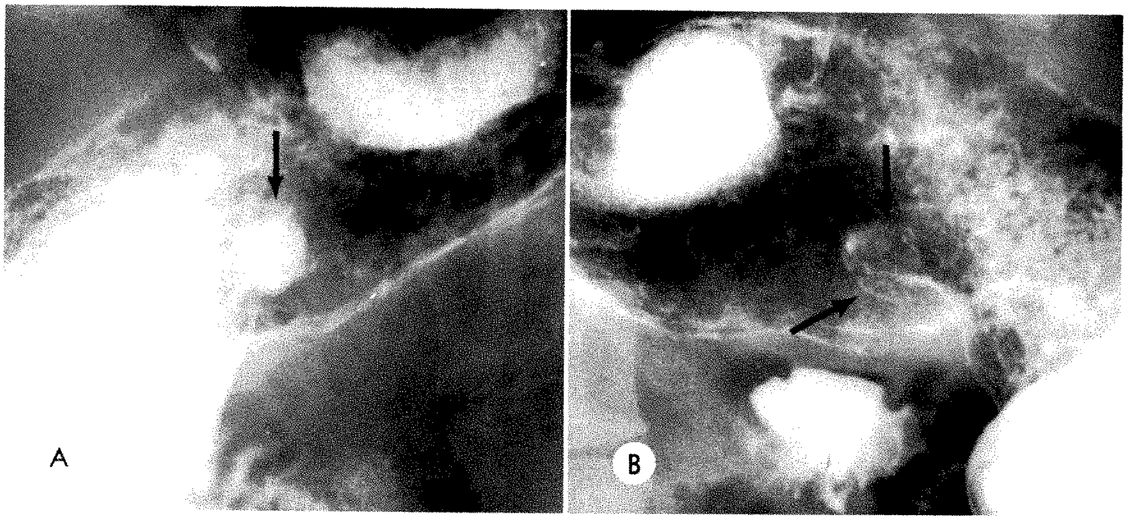


Fig. 5. (*A*) Gas distended stomach, with lesser curvature dependent, showing barium-filled ulcer (arrow). (*B*) Gas distended stomach with greater curvature dependent and the ulcer, now superior, shows as a ring (arrows).

evidence that an ulcer is present. In some cases the use of special manipulations may then make it possible to demonstrate the ulcer filled with barium, en face or in profile. In a few cases, however, the ring may remain as the only reasonably certain evidence that a crater exists (Fig. 9).

If two ulcers are present and are on opposite walls, the one on the posterior wall will be filled with barium in the supine position. The one on the anterior wall may be overlooked unless a ring is looked for in the air study (Fig. 10, *A* and *B*). When it is possible to trap air in the bulb with the patient prone (and this may be difficult), the appearance of the ulcers will be reversed; the ring now becomes a fleck, and the fleck, a ring.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis between benign and malignant ulcers is still a difficult roentgenologic problem. Combined air distention and barium studies are some-

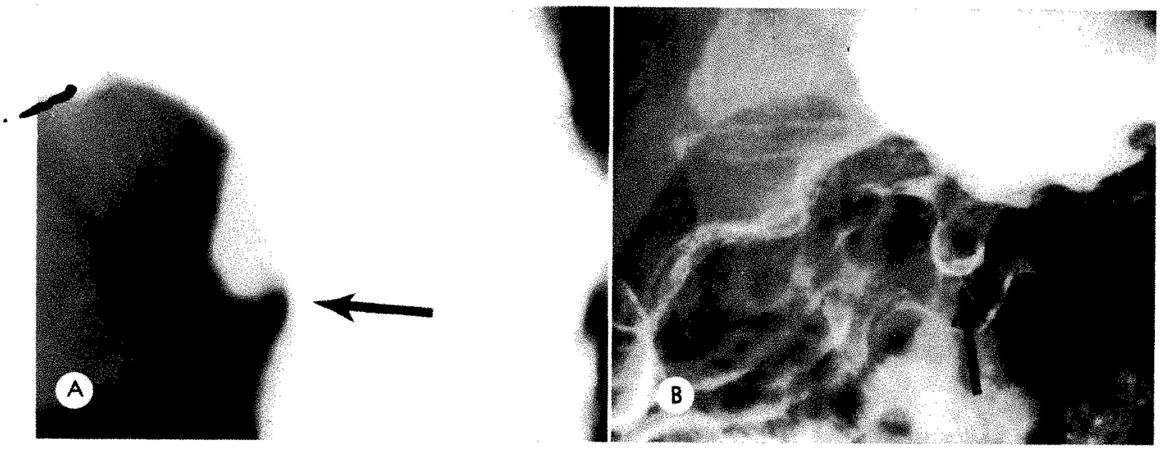


Fig. 6. It is essential that the barium impregnated ulcer wall be tangential to the ray in order to form a ring. (*A*) Ulcer with one sloping and one vertical wall (arrow). (*B*) In gas distended stomach only partial ring is seen (arrow).

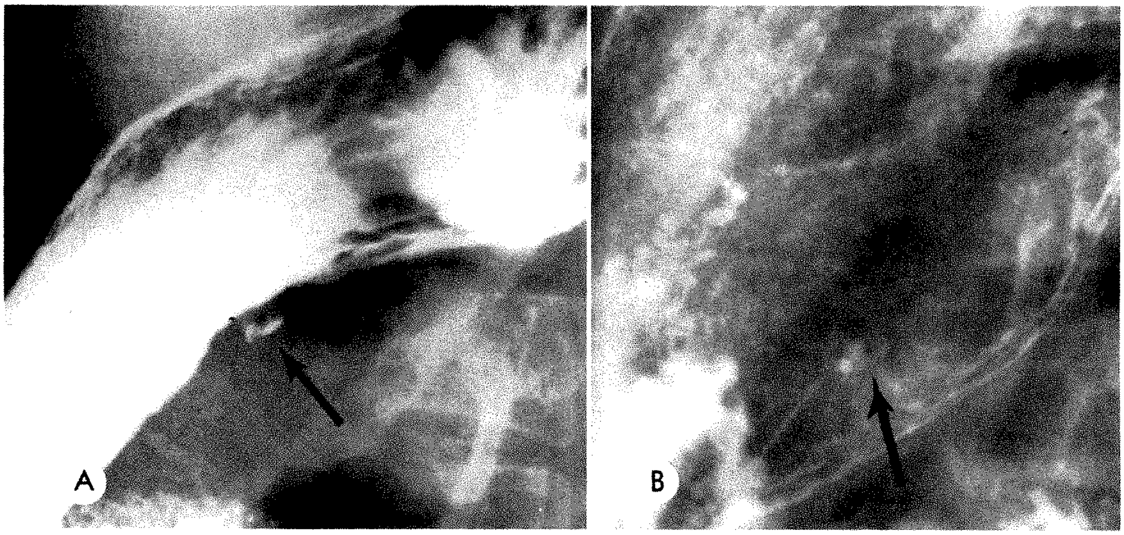


Fig. 7. (*A*) High posterior wall gastric ulcer was seen only on this one roentgenogram (arrow). No better visualization with attempted refilling. (*B*) Confirmed on gas distention study as a ring (arrow).

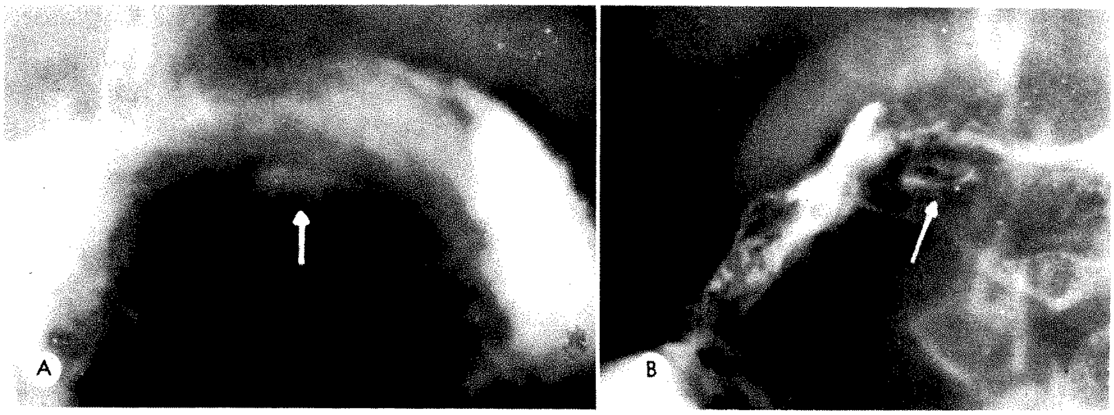


Fig. 8. (*A*) Linear barium fleck seen in distorted, flattened bulb (arrow). Pressure deformity was due to carcinoma of pancreas. Profile view was impossible. (*B*) Ring, conforming to the shape of barium fleck appears on gas distention study (arrow). Benign linear ulcer confirmed at autopsy.

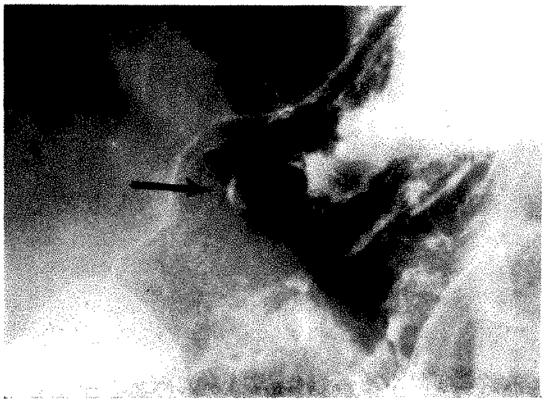


Fig. 9. Hematemesis in young adult. Gas distention study reveals a linear "ring," confirmed as crater by gastroscopy (arrow). Impossible to show as barium filled crater.

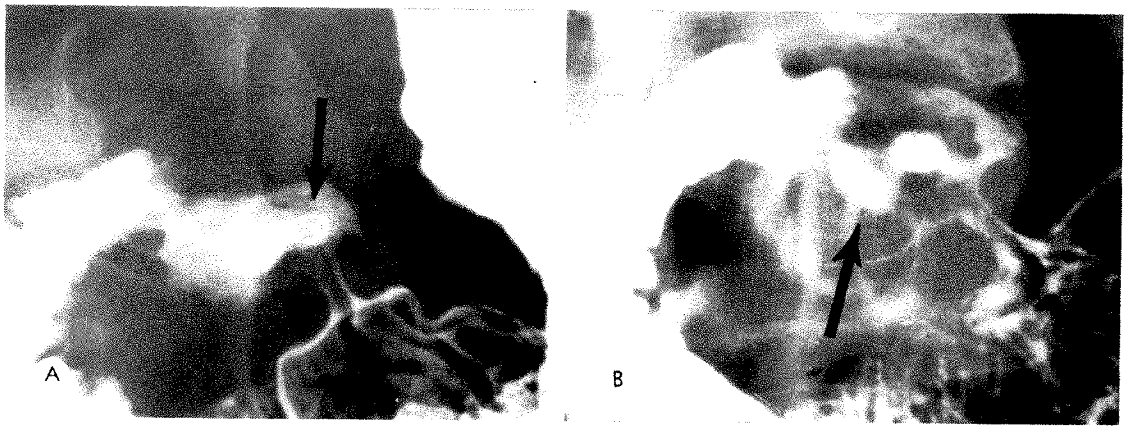


FIG. 10. (*A*) Two duodenal ulcers. With patient supine the posterior wall ulcer is barium filled and the anterior wall ulcer is seen as a ring (arrow). (*B*) With patient prone and air trapped in bulb, the anterior wall ulcer is now dependent and is barium filled. The posterior wall ulcer is superior and is less well filled (arrow).

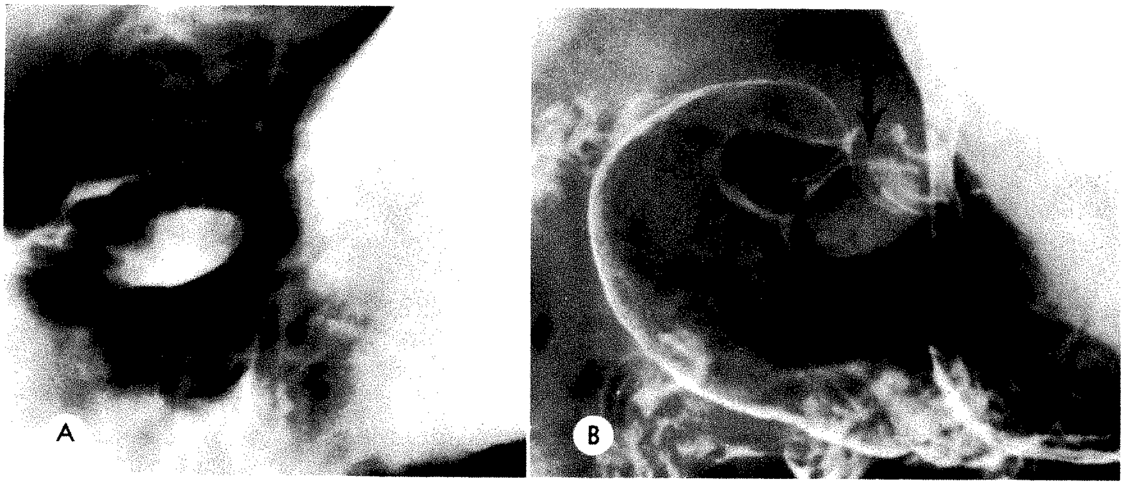


FIG. 11. (*A*) Compression study of large, benign gastric ulcer which does not project definitely beyond the stomach wall. Irregular thickened collar. (*B*) Gas distention study shows sharply defined crater edges without surrounding irregularities (arrows).

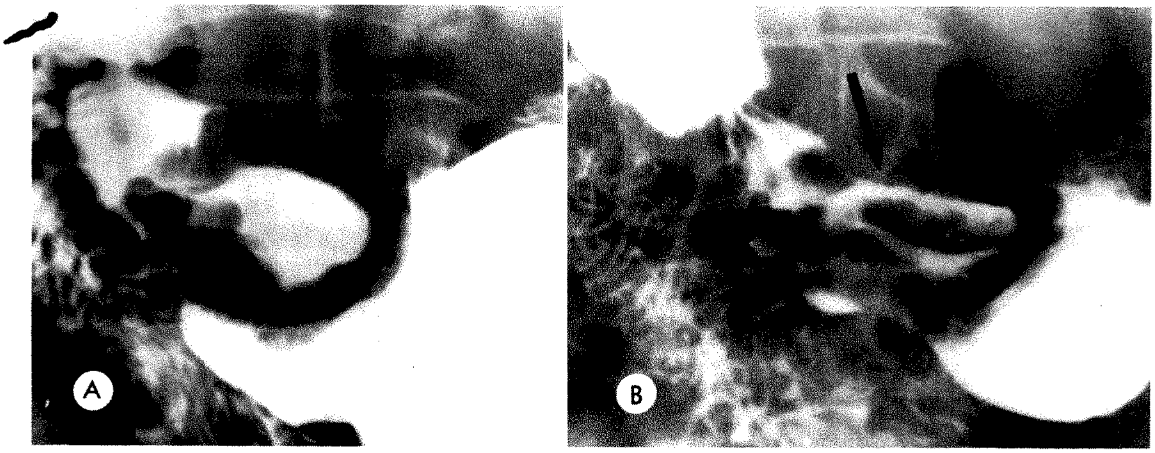


FIG. 12. (*A*) Malignant gastric ulcer presenting as shallow crater with surrounding irregular collar. (*B*) With air contrast ulcer maintains shape and resembles a gastric fold (arrow). Irregular collar remains.

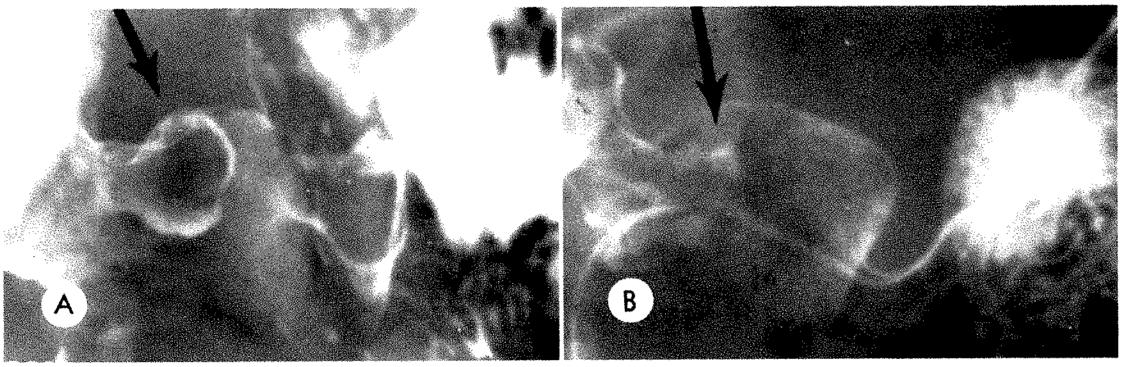


Fig. 13. (*A*) Antral ulcer demonstrated as a ring (arrow). (*B*) After medical therapy gas distention study shows persistent ulcer as a minute ring (arrow).

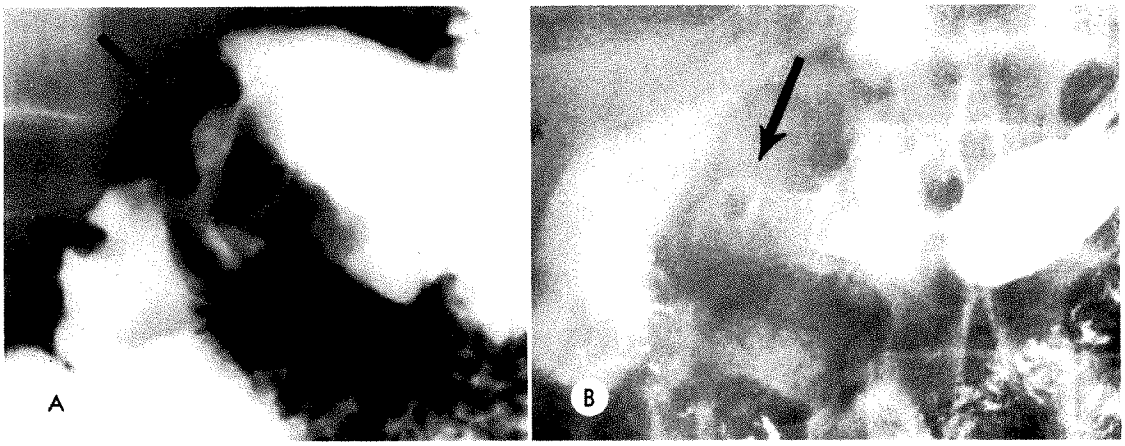


Fig. 14. (*A*) Postbulbar ulcer seen as barium filled crater (arrow). (*B*) Review of earlier study shows ring (arrow) as only evidence that ulcer was present at that time.

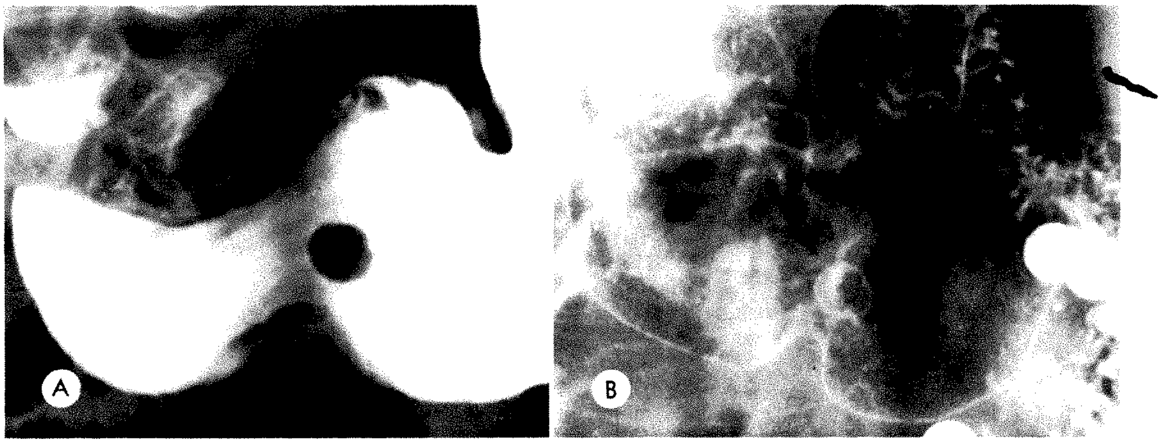


Fig. 15. (*A*) Gastric polyp seen as filling defect. (*B*) Double contrast study shows the polyp as a ring (arrow).

times helpful in the solution of certain puzzling situations. The gas distention will flatten prominent folds in some cases and clarify the relationship between the crater and the surrounding area. The malignant ulcer, just as the benign one, will trap air and should not be mistaken for a prominent fold. It should be studied with the same care as when barium filled (Fig. 11, *A* and *B;* and 12, *A* and *B*).

When ulcers become smaller during the healing phase, they may become difficult to detect or to distinguish from areas of crossing folds. Distention studies will obliterate the latter and perhaps open the ulcer up to some degree. If the ulcer is unhealed and therefore has a granulating surface which holds barium, it may trap enough to show as a minute ring (Fig. 13, *A* and *B*). It is conceivable that this may differentiate between a mucosa covered shallow "pit" and an incompletely healed ulcer.

When one is responsible for the work of others, as in consultations or in supervising the work of residents, roentgenograms must be viewed without benefit of fluoroscopy and manipulation. It is comforting to see certain questionable projections from the wall of the stomach or duodenum or certain dubious en face niches confirmed in double contrast studies as rings (Fig. 4, *A* and *B;* and 8, *A* and *B*). Also where previous studies are reviewed in the light of a current diagnosis of ulcer, a ring may be the only evidence that a lesion actually was present on an earlier examination (Fig. 14, *A* and *B*).

One must be careful that artifacts, normal channels on end (such as the pyloric canal and the apex of the bulb), axial views of peristaltic contractions, polyps (as seen in gas distention studies, Fig. 15, *A* and *B*) and diverticula are not mistaken for ulcer "rings." Careful observation will reveal the true nature of these shadows.

It is obvious that ulcerating lesions elsewhere in the gastrointenstinal tract may be seen as rings in accordance with the principles already stated.

CONCLUSIONS

In our experience the recognition of the ulcer "ring" has been extremely helpful in:

1. Confirmation, location and detection of an ulcer.
2. Detection of more than one ulcer.
3. Differentiation between benign and malignant gastric ulcer.
4. Determination of complete healing of an ulcer.
5. Consultation with other radiologists and review of work done by residents.
6. Retrospective studies.

George R. Krause, M.D.
Mount Sinai Hospital of Cleveland
University Circle
Cleveland 6, Ohio

REFERENCES

1. HAMPTON, A. O. Safe method for roentgen demonstration of bleeding duodenal ulcers. AM. J. ROENTGENOL. & RAD. THERAPY, 1937, *38*, 565–570.
2. MEUWISSEN, T. J. J. H. X-Ray Atlas and Manual of Esophagus, Stomach and Duodenum. Elsevier Press, Inc., Amsterdam, Netherlands, 1955.
3. SCHATZKI, R., and GARY, J. E. Face-on demonstration of ulcers in upper stomach in dependent position. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1958, *79*, 772–780.
4. TEMPLETON, F. E. X-Ray Examination of the Stomach. University of Chicago Press, Chicago. 1944.

GASTROESOPHAGEAL RETROGRADE MUCOSAL PROLAPSE*

A CAUSE OF UPPER GASTROINTESTINAL HEMORRHAGE

By CHARLES J. FAGAN, CAPTAIN, MC, US ARMY *and* EDDY D. PALMER, COLONEL, MC, US ARMY
FORT SAM HOUSTON, TEXAS

DETECTION and identification of the responsible lesion in the patient with upper gastrointestinal hemorrhage are in most instances the result of roentgenographic and endoscopic effort. Diagnostic effectiveness depends to a large degree on knowledge of both the common and the rare explanations for hemorrhage. Gastroesophageal retrograde mucosal prolapse, an infrequently reported condition, can give rise to significant hematemesis. It is our purpose to describe 2 cases (one previously reported) of this entity associated with upper gastrointestinal hemorrhage.

REPORT OF CASES

Case i. R.C., a Caucasian female aged 47, was admitted to the hospital an hour after she vomited about a pint of bright red blood. She gave a 31 year history of numerous abrupt episodes of distress, "like a knot," beneath the xiphoid. Each episode was regularly accompanied by temporary inability to swallow. Swallowing immediately became easy when the sensation of the "knot" abated. There had not previously been recognized gastrointestinal bleeding. At the time of admission, the patient stated that she had been experiencing the above symptoms repeatedly for at least 5 days.

Examination demonstrated the signs of acute and chronic blood loss. There was extreme obesity. The hematocrit was 24 per cent and hemoglobin 5.5 gm. A nasogastric tube was passed to a point of obstruction in the lower esophagus; aspiration here delivered fresh and old blood. Resuscitative measures included transfusion of 1,500 ml. of whole blood.

Emergency upper gastrointestinal roentgen study, performed after the nasogastric tube had been removed, disclosed an obstructing lesion in the distal esophagus at the gastroesophageal junction. This lesion (Fig. 1, *A* and *B*) was characterized by a positive radiolucent filling defect within the barium column. The esophageal lumen in the region of the mass was well outlined, and the surrounding esophageal wall was found to be free of stricture, spasticity, and irregularity. A hiatus hernia was also present. The barium suspension failed to pass beyond the esophageal lesion into the stomach, in spite of supine, prone, and semi-standing positioning.

Esophagoscopy performed 8 hours after the upper gastrointestinal roentgen study disclosed a large plug of gastric mucosa filling the distal esophageal lumen. No barium remained in the esophagus. The plug's surface was angry, edematous, eroded and actively bleeding. The immediate impression was fungating carcinoma, but, as the blood was being aspirated and biopsies were being taken, the mass migrated distally and disappeared circumferentially as part of the gastric wall. A 4 cm. direct hiatus hernia was then apparent. The esophageal mucosa was entirely normal, but all of the herniated gastric mucosa was eroded and bleeding. It was clear that the mass had represented a sleeve of gastric mucosa which had prolapsed upward into the esophageal lumen. The biopsy specimens subsequently were interpreted as acute erosive gastritis.

Upper gastrointestinal roentgen examination was repeated on the third hospital day. The barium suspension was seen to move freely through the distal esophagus into the stomach (Fig. 2, *A* and *B*). The previously noted polypoid filling defect was now absent. Roentgenographic evidence of a hiatus hernia was still present.

The patient's subsequent hospital course was uneventful. Various routine and special laboratory tests were within normal limits. A barium enema examination was negative. It was thought that surgical repair of the hiatus hernia might prevent the periodic prolapse but the severe obesity precluded immediate consideration of this move. She is now undergoing controlled weight reduction.

Case ii (previously reported[16]). This 33 year

---

* From the Radiology and Gastroenterology Services, Brooke General Hospital, Fort Sam Houston, Texas.

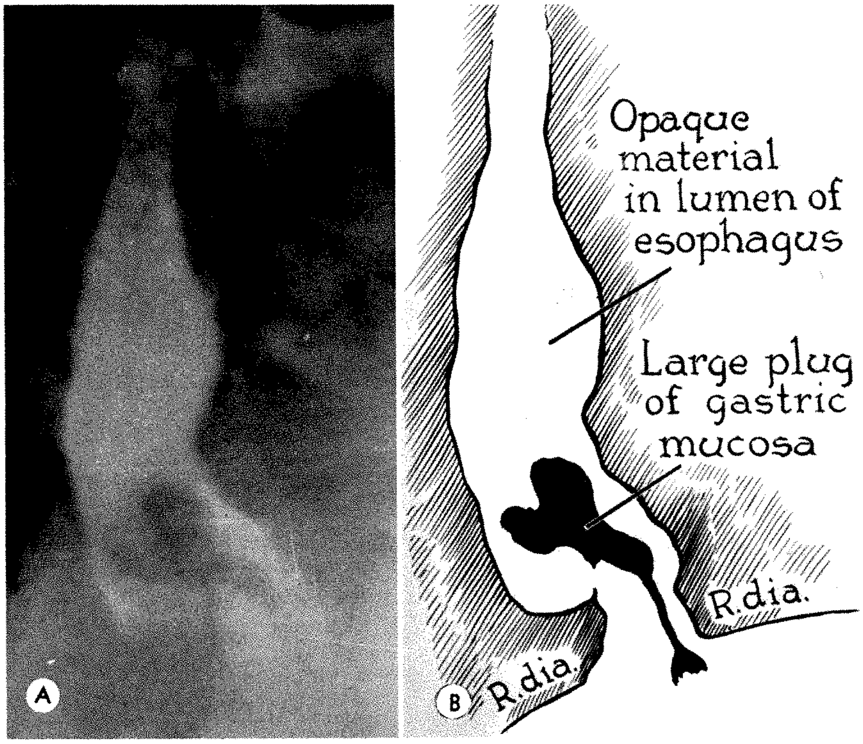

Opaque material in lumen of esophagus
Large plug of gastric mucosa
R.dia.
R.dia.
A
B

Fig. 1. Case 1. (*A*) Spot roentgenogram of the lower third of the esophagus taken in the right anterior oblique position demonstrates a positive radiolucent defect within the barium column. The surrounding esophageal wall is free of stricture, spasticity, and irregularity. This lesion, a large plug of gastric mucosa, prevented the passage of barium into the stomach. The hiatus hernia is not seen. (*B*) Line drawing of the spot roentgenogram.

old Caucasian male was hospitalized after having vomited small amounts of blood for 3 days. The first upper gastrointestinal roentgen examination was normal. Esophagoscopically, the esophagus was normal and the esophagogastric junction was in the proper position, but each time the patient retched or gagged the gastric mucosa appeared suddenly as a plug within the distal esophagus and slowly squeezed itself about 5 cm. proximally. The plug could easily be pushed back into the stomach with the esophagoscope, and then it was seen that it represented a sleeve of gastric mucosa. The prolapsed gastric mucosa was intensely hyperemic and bled slowly. Repeat roentgenologic studies succeeded in demonstrating gastroesophageal retrograde prolapse. The prolapse could be induced by a Valsalva maneuver and reduced by a swallow of barium suspension.

DISCUSSION

The anatomy and physiology of the cardia are such that mechanical displacements, prolapses and intussusceptions can occur easily. Except for hiatus hernia, however, mechanical disorders are uncommon or even rare. In cases reported in the literature, it is often difficult to determine exactly what defect is being described, even when reproductions of the roentgenograms are presented. The problem is, of course, that this is a notably dynamic area, and, when the regional tissues loosen up, various displacements may alternate with each other.

Next to hiatus hernia, the commonest displacement appears to be prograde prolapse of a sleeve of esophageal mucosa into the gastric lumen.[5,8,9,14,16,18–22] In many of these cases hiatus hernia is also present. This is wholly a roentgen diagnosis, being inapparent to the esophagoscopist. It ordinarily is thought of as having no clinical significance, although, strangely, the instance described by Sarasin and Hoch[22] appeared to be associated with a degree of distal esophageal stenosis.

Much less commonly, the esophageal prolapse is initiated proximal to the cardia so that the sliding mucosa remains within the esophageal lumen.[10–13] This is, then, an esophagoesophageal prograde prolapse. It, too, appears to be associated ordinarily with hiatus hernia, and the buckling of the mucosa, together with contraction of the esophageal longitudinal muscle layer, produces the picture of shortened esophagus.

Retrograde invaginations at the cardia are not as common, which is interesting in view of the fact that the diaphragm separates an area of positive pressure below from a vacuum above. A few instances of partial retrograde gastroesophageal intussusception have been described,[2,6] and in another case[7] a gastric diverticulum had turned inside out and then prolapsed upward into the esophagus.

Retrograde prolapse of a sleeve of gastric mucosa into the esophageal lumen has been described at least 14 times, as best we can determine.[1,3,8,16,17,23–25] The clinical aspect most frequently emphasized has been intermittent lower esophageal obstruction, a dramatic feature in our experience. Small amounts of bleeding have been reported,[3,16] but the magnitude of the hemorrhage in Case I appears to be unique. By esophagoscopic examination during active bleeding, we were able to show that the herniated plug of gastric mucosa was the source, both while the mucosa was displaced proximally and after it had returned to its normal position in the sac of the hiatus hernia.

Hiatus hernia has been a frequent accompaniment of retrograde prolapse, although not to the point of being a characteristic feature of the condition. The hernia adds to the difficulty of making an accurate interpretation of both the roentgen and the endoscopic findings. The differential diagnostic problems that gave us most trouble were distal esophageal tumor and foreign body.

SUMMARY

Two cases of retrograde prolapse of the gastric mucosa at the esophageal gastric junction (one previously reported) have been presented, together with a brief survey of the literature of mucosal and mural

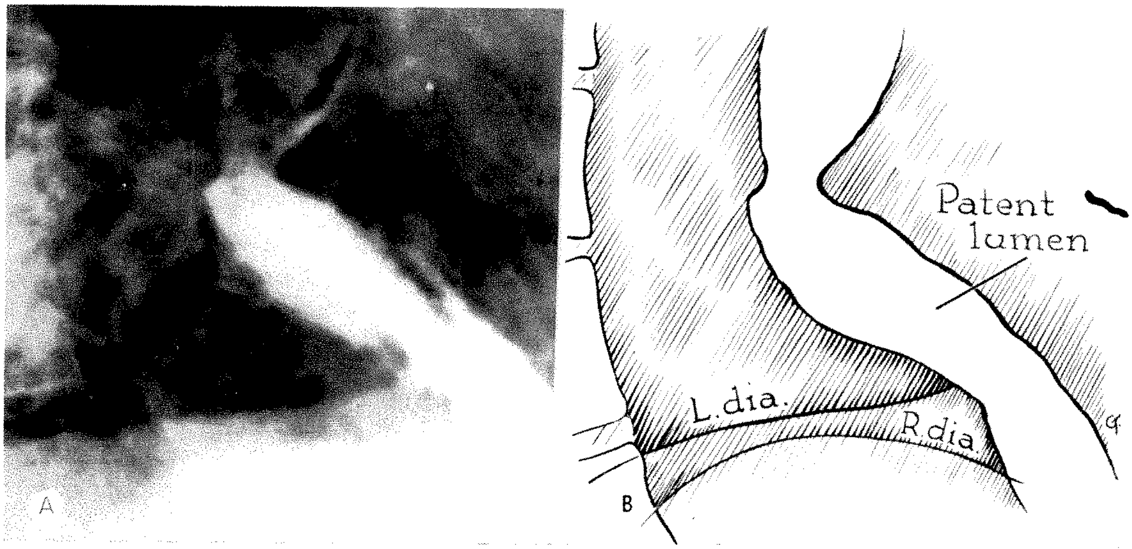


Fig. 2. Case I. (*A*) Spot roentgenogram of the lower third of the esophagus taken in the right anterior oblique position during the repeat gastrointestinal study demonstrates free flow of the barium suspension through the esophagus into the stomach. The previously present gastric mucosa filling defect is absent. (*B*) Line drawing of the spot roentgenogram.

displacements at the cardia. Emphasis has been placed on significant acute and chronic blood loss as a complication of this entity. In our opinion, gastric mucosa which has prolapsed into the lower esophagus can readily be confused with a neoplastic process and with foreign body.

Charles J. Fagan, Captain, MC
Gorgas Hospital
Box 0
Balboa Hts. Canal Zone

REFERENCES

1. Blum, S. D., Weiss, A., Weiselburg, H. M., and Siegel, W. B. Retrograde prolapse of gastric mucosa into esophagus. *Gastroenterology*, 1961, *41*, 408–411.
2. Enderlen. Invagination der vorderen Magenwand in den Oesophagus. *Deutsch. Ztschr. Chir.*, 1903, *69*, 60–66.
3. Feldman, M. Retrograde extrusion or prolapse of gastric mucosa into esophagus. *Am. J. M. Sc.*, 1951, *222*, 54–60.
4. Haering, R. Magenschleimhautprolaps in den Oesophagus als seltene Ursache einer Dysphagie. *Chirurg*, 1961, *32*, 115–119.
5. Klinefelter, E. W. Invagination of esophagus in hiatus hernia. *Radiology*, 1956, *67*, 562–567.
6. Lannon, J., and Culiner, A. Retrograde intussusception of lesser curvature of stomach, pylorus, and first part of duodenum into oesophagus. *Brit. J. Surg.*, 1946, *33*, 392–393.
7. Liaras, and Ricard, E. Dilatation circonférentielle de l'oesophage médiastinal par invagination partielle gastro-oesophagienne. *Ann. anat. path.*, 1934, *11*, 868–872.
8. de Lorimier, A. A., and Warren, J. P. Prolapse of mucosa at esophagogastric junction. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1960, *84*, 1061–1069.
9. Lutz, P. Invagination der Oesophaguswand. *Med. Klin.*, 1960, *55*, 2373–2375.
10. Malenchini, M., and Resano, J. H. Hernia hiatal tipo III descubierta radiológicamente por la invaginación eso-esofágica. *Prensa méd. argent.*, 1954, *41*, 3705–3708.
11. Malenchini, M., and Resano, J. H. Invaginación eso-esofágica que simula un esófago corto en una hernia hiatal tipo III. *Prensa méd. argent.*, 1954, *41*, 3787–3790.
12. Malenchini, M., and Resano, J. H. Seudoesófago corto congénito por invaginación del esófago abdominal en el esófago toracico de una hernia hiatal de tipo III de Åkerlund. *Prensa méd. argent.*, 1954, *41*, 3861–3863.
13. Malenchini, M., and Resano, J. H. Hernia hiatal tipo III oculta por invaginación esofágica que simula un esófago corto. *Prensa méd. argent.*, 1955, *42*, 51–52.
14. Malenchini, M., and Resano, J. H. Valor diagnóstico radiologico de la insuflación de la cámara aérea para el diagnóstico diferencial de los tumores del tercio superior del estómago. *Prensa méd. argent.*, 1955, *42*, 1204–1207.
15. Ödegaard, H. Invagination of esophagus in hiatus hernia: report of 8 cases. *Acta radiol.*, 1959, *51*, 443–448.
16. Palmer, E. D. Mucosal prolapse at the esophagogastric junction. *Am. J. Gastroenterol.*, 1955, *23*, 530–537.
17. Paulino, F., and Aprigliano, F. Prolapso da mucosa gástrica através o cárdia. *Rev. brasil. cir.*, 1956, *32*, 487–489.
18. Perotti, F. Ernie dello iato e prolasso del cardias. *Radiol. med.*, 1956, *42*, 765–771.
19. Poirier, A., and Poirier, B. Invagination de l'esophage dans la hernie diaphragmatique de l'estomac. *Arch. mal. app. digest.*, 1954, *43*, 610–612.
20. Sarasin, R., and Hoch, A. Die Invagination der Oesophagusschleimhaut in den Magen. *Schweiz. med. Wchnschr.*, 1951, *81*, 1207–1209.
21. Sarasin, R. Les invaginations oesophagogastriques. *Radiol. clin.*, 1952, *21*, 391–394.
22. Sarasin, R., and Hoch, A. Les invaginations oesophagogastriques. *Arch. mal. app. digest.*, 1952, *41*, 434–440.
23. Starr, K. W. Cardio-oesophageal intussusception and operative cure. *M. J. Australia*, 1955, *42*, 683–684.
24. Weiss, K. Zur Kasuistik ösophagealer Schluckstörungen. *Kinderärztl. Praxis*, 1950, *18*, 429–433.
25. Wells, J. Herniation of gastric mucosa into esophagus: report of case. Am. J. Roentgenol. & Rad. Therapy, 1947, *58*, 194–195.

DIAGNOSTIC PROBLEMS OF ESOPHAGEAL CANCER*

RELATIONSHIP TO ACHALASIA AND HIATUS HERNIA

By WILLIAM B. SEAMAN, M.D., JOSEPHINE WELLS, M.D., *and*
CHARLES A. FLOOD, M.D.
NEW YORK, NEW YORK

THE coexistence of two or more lesions usually presents a difficult problem in differential diagnosis. This is even more apt to be true when one condition is capable of simulating another. We have been interested in the association of lower esophageal cancer with achalasia and hiatus hernia particularly because of recent evidence suggesting that the two latter conditions may predispose toward malignant transformation.[1,10,15,25,28,38,39,42,49] The classic teaching is that esophageal dilatation proximal to a malignant constriction is slight or absent since the duration of the carcinoma is usually too short for it to develop. Achalasia, on the other hand, is characterized by moderate to marked dilatation and a smoothly tapering distal esophagus terminating at the gastric cardia. Although the esophagus is frequently quite tortuous in achalasia, earlier in the course of the disease it may be straight and only moderately dilated. This appearance may be simulated by tumors arising in the distal esophagus or gastric fundus and present a difficult diagnostic problem.[3,12,27,30,50]

ACHALASIA AND ESOPHAGEAL CANCER

Extensive tumors of the gastric fundus may be manifest by encroachment of the air filled fundus (Fig. 1, *A* and *B*), an increased

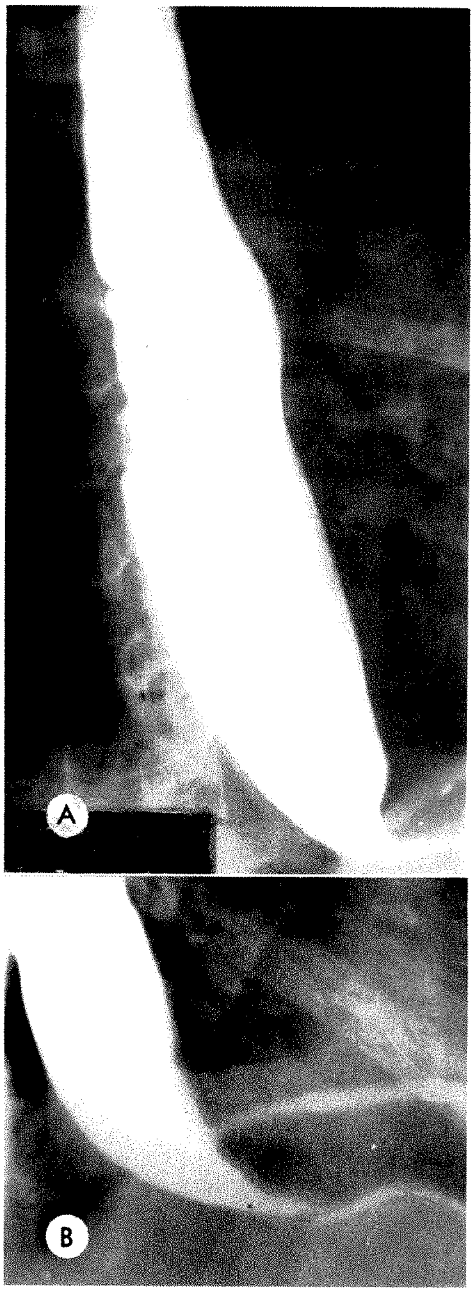


FIG. 1. J.W. (65-59-56). (*A*) Dilated esophagus with smooth tapering in distal portion simulating achalasia. (*B*) Carcinoma diagnosed by fundal mass outlined with barium.

---

* From the Departments of Radiology and Medicine, College of Physicians and Surgeons, Columbia University, and Presbyterian Hospital, New York, New York.

Presented at the Sixty-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 2-5, 1962.

ration will usually suggest the diagnosis of achalasia. However, Lawrence and Shoesmith,[26] in a study of 137 patients with achalasia, found that 16 had symptoms of less than 12 months' duration. Onset late in life is more characteristic of esophageal cancer than achalasia, but achalasia can begin in the later years. Forty-nine (35 per cent) of the 137 patients reported by Lawrence and Shoesmith were over the age of 50 years. Ellis,[15] studying the natural history of achalasia, found only 2 of 33 patients in whom the age of onset was in the fifth decade.

The diagnosis of achalasia probably should not be accepted until carcinoma of the distal esophagus or stomach is excluded and sensitivity to parasympathomimetic drugs is demonstrated, although the latter is not invariable even in the early stages. Inflammatory lesions, such as peptic esophagitis, have been reported to produce achalasia,[49] so it is conceivable that the myenteric nerve plexus might be destroyed by carcinomatous infiltration and result in achalasia. The following 2 cases are examples of esophageal cancer that were initially considered as achalasia because of their clinical and roentgenologic manifestations:

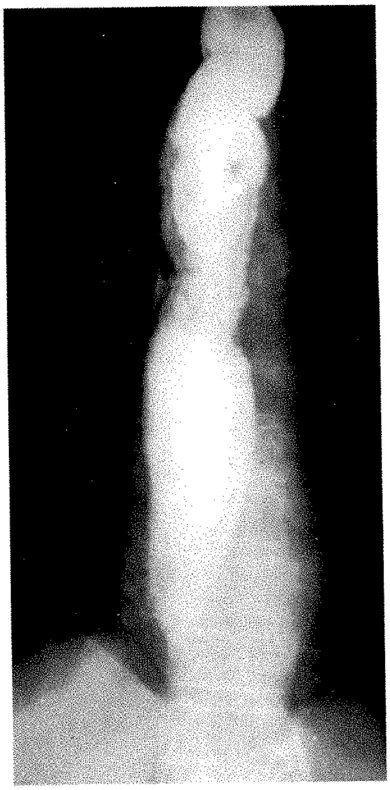


Fig. 6. Case 1. C.H. (65-03-28). Markedly dilated esophagus in a 75 year old male with dysphagia for 3 months. Note retained food particles and absence of gastric air bubble. Other views demonstrated a smooth tapering distal esophagus extending to the cardia. Well differentiated adenocarcinoma of distal esophagus was found at autopsy.

Case 1. C.H. (65-03-28), a 75 year old white male, entered the hospital because of vomiting and dysphagia. Three months prior to hospital admission he first noted the gradual onset of dysphagia for solid foods. One month later he began to vomit, both clear mucus and food, during and immediately after eating. The vomiting increased in both frequency and severity until hospitalization became necessary.

Chest roentgenograms revealed bilateral bronchopneumonia probably due to aspiration. An air fluid level was noted behind the trachea on the lateral chest roentgenogram. On esophagoscopy, the esophagus was found to contain copious amounts of fluid and solid foods. Intubation of the esophagus met with resistance at the level of the cardia but after a wait of 1 minute, the bougie slipped easily into the stomach. This seemed to confirm the clinical impression of achalasia. Roentgen examinations demonstrated a markedly dilated esophagus with considerable quantities of retained food and secretions (Fig. 6). Dilatation of the cardia on three occasions produced only transient improvement in swallowing. The dysphagia was also thought to be partially due to neuromuscular dysfunction resulting from cerebral arteriosclerosis. The patient's general condition steadily deteriorated and the mixed pulmonary infection was unresponsive to antibiotics. Continued weight loss, accompanied by oliguria, anemia and hypoproteinemia continued until death occurred 7 weeks after admission.

At autopsy the esophagus was found to be dilated but without muscular hypertrophy. At the lower end a hard annular mass markedly narrowed the lumen. The mucosa in this area was diffusely thickened for a distance of approxi-

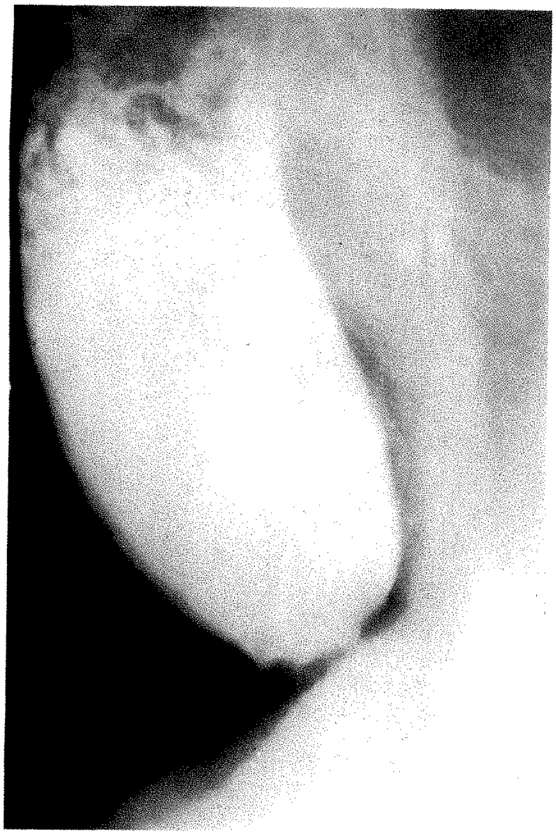


FIG. 7. Case II. N.A. (142-37-10). Dilated esophagus in a 67 year old male with an 18 month history of dysphagia. Note absence of gas in the stomach and the irregular contour of the distal esophagus. A well differentiated epidermoid carcinoma was detected by esophagoscopy.

mately 2 cm. below and 5 cm. above the esophagogastric junction. A 1 cm. elevated nodule was found in the center of the indurated area. Areas of anaplastic and well differentiated adenocarcinoma were seen on histologic examination.

CASE II. N.A. (142-37-10), a 67 year old male, for 18 months had had difficulty swallowing both liquids and solids, accompanied by nausea, eructation, regurgitation, and epigastric fullness. These symptoms increased in severity and frequency and became associated with anorexia and a 30 lb. weight loss. Nine months earlier, a fluoroscopic examination performed elsewhere was said to disclose a stenosis of the distal esophagus with proximal dilatation. Bouginage was carried out several times but without relief.

Roentgenographic examinations performed here (Fig. 7) outlined a dilated esophagus with retained food. A significant amount of barium was still present in the esophagus several hours later. Detailed views of the lower esophagus revealed asymmetry but smooth contours. The roentgenographic impression was achalasia with partial obstruction.

Esophagoscopic biopsies of red granular mucosa at the lower esophagus were positive for cancer. At operation a well differentiated adenocarcinoma of the stomach and distal esophagus was found.

An even more difficult diagnostic problem is presented by the development of a carcinoma in a patient with true achalasia. In 1961, Tanner and Smithers[49] were able to collect 40 examples of this association from the literature and we have been able to find 32 additional cases including 4 from this institution (Table I). It is felt by many that achalasia with its prolonged associated

TABLE I

ACHALASIA AND ESOPHAGEAL CANCER

Author	Upper Third	Middle Third	Lower Third	Incidence
Tanner and Smithers[49]	5	25	10	
Lawrence and Shoesmith[26]	2		1	2.0%
Camara-Lopes[10]		5	2	6.6%
Kay and Cross[25]		1		1.5%
Seaman, Wells and Flood		3	1	
Ellis[15]	7—site not stated			8.0%
Virno and Carboni[50]	1			0.8%
Santy, Michaud and Viard[40]	7			4.0%
Hoover[23]	2			1.5%
	Total—72 cases			

esophagitis and food retention predisposes to malignant change although the actual frequency is difficult to ascertain.[10,25,38,52] Only a few authors give incidence rates and these vary from 1.5 per cent to 8 per cent.[10,15,23,25,26,40,50] Ellis,[15] in a follow-up study of 85 patients with achalasia, found that 7 of the 24 deaths were due to carcinoma. Camara-Lopes[10] reported 7 cases of carcinoma occurring in a group of 90 cases of mega-esophagus. Since the death rate for carcinoma of the esophagus in the general population at age 65 ranges from 25 to 57 per 100,000 for males, and 9 to 35 per 100,000 for females, there does seem to be a predilection for this disease in patients with achalasia. Cancer of mega-esophagus develops only in long-standing cases (an average of 18 years) so that its incidence in a given series may depend on the duration of the follow-up study.

The major points of interest about carcinomas associated with achalasia are that they usually involve the middle third of the esophagus and are predominantly epidermoid carcinomas, although an occasional adenocarcinoma has been reported. They tend to occur at a younger age (average 52 years) than the average for all esophageal cancer (average 64.6 years). Since the esophagus is already dilated, obstructive symptoms are rare unless the tumor occurs at the distal esophagus. They are rarely detected roentgenologically, since the filling defect is usually misinterpreted as retained food. In patients with achalasia the roentgenologic examination should be done only after thorough esophageal lavage and the midesophagus should be examined very carefully because of the predilection of this area for malignant degeneration. Our experience with this complication is limited to 4 cases.

Case III. H.C. (142-97-40), a 52 year old white female with a 32 year history of achalasia, was admitted to the hospital for esophagoscopy because of chest pain and blood streaked regurgitation of several weeks' duration. From the 28 cm. to the 38 cm. level the endoscopist observed a granular, reddened mucosa that bled easily and suggested the diagnosis of chronic esophagitis with superficial ulcerations. Roentgenographic examination showed slight dilatation of the proximal one-third of the esophagus. From the level of the aortic arch to a few centimeters above the diaphragm, the esophageal contour was irregular and ill-defined; again suggestive more of inflammation than neoplasia. A diverticulum was noted at the junction of the middle and lower third of the esophagus (Fig. 8).

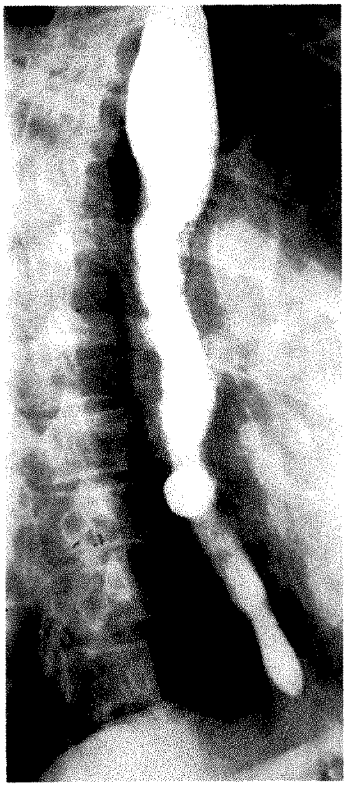


Fig. 8. Case III. H.C. (142-97-40). A 52 year old female with a 32 year history of achalasia had a spreading type of carcinoma involving almost the entire distal two-thirds of the esophagus. Note the *en face* view of a diverticulum at the junction of middle and lower thirds. The absence of significant dilatation or constriction makes the diagnosis of either achalasia or carcinoma difficult.

She was treated by bouginage and aspirations for several weeks until pathologic studies of fluid aspirated from the esophagus showed the presence of malignant cells. Surgical resection was carried out. Pathologic examination disclosed an extensive flat carcinoma composed of undifferentiated cells. The upper limit showed intramucosal invasion.

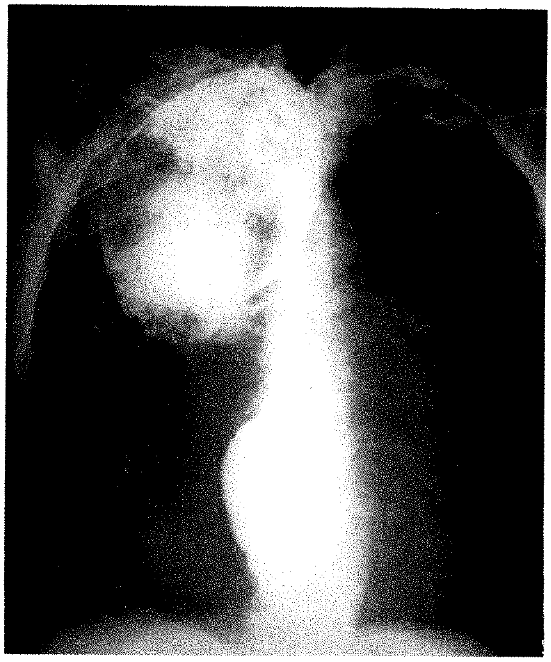


Fig. 9. Case vi. S.A. (144-45-88). Carcinoma of the mid-esophagus occurring in an elderly male with a 25 year history of achalasia. Disproportionate dilatation of proximal third has been noted in patients with uncomplicated achalasia. Tumor cannot be identified even in retrospect.

Comment. This was a rather unusucal gross pathologic type of esophageal carcinoma. Stout and Lattes[47] state that there do not seem to be any carcinomas in the esophagus exactly comparable to the superficial spreading variety found in the stomach. However, they do mention a case reported by Gauthier-Villars and Dontzoff in which the cancer started on one side and grew spirally as it descended.

Case iv. D.L. (82-46-31), a 38 year old male, was first seen because of a pain in the epigastrium and lower chest without relation to meals. For 28 years, since the age of 10, he had had difficulty in getting food to go down into his stomach. Roentgenograms showed a markedly dilated esophagus for its entire length with residual fluid, thought to be typical of achalasia. Gastric lavage revealed over 500 cc. of retained food and bloody mucus. He was hospitalized briefly and treated with gastric lavage followed by dilatation.

One year later, he was again admitted to the hospital when it was noted that he had continued to have a dull aching epigastric pain radiating to the left shoulder since his last hospital admission. At this time, the medical consultant's note stated, "a characteristic that is unusual in cardiospasm has been the persistent serosanguineous foul smelling material mixed with thick mucus and the constant sternal pain." Because the patient had an elevated temperature at this time, it was thought that he might have esophagitis or a peri-esophagitis. Re-examination by roentgenographic techniques revealed the esophagus to be slightly smaller than the year before and flexible. There was nothing to suggest carcinoma. The sedimentation rate at this time was 73 mm./hr. Roentgenograms of the chest showed evidence of bilateral aspiration pneumonia.

Because of persistence of pain, he was again esophagoscoped and a large fungating grayish mass was seen 2 cm. from the distal end of the esophagus arising from the left side. The biopsy showed this to be a squamous cell cancer of the esophagus.

At the time of surgery a large firm lobulated mass was present in the upper thoracic esophagus extending from a point just below the aortic arch to the thoracic inlet. It evidently originated from the esophagus just above the aortic arch and in this area infiltrated the mediastinal tissues widely to include the wall of the superior surface of the aortic arch.

Case v. E.M. (65-93-27), a 48 year old female, had had recurrent episodes of difficulty in swallowing and regurgitation ever since her first pregnancy 20 years before. Five years earlier, because of characteristic roentgen and clinical findings, a diagnosis of achalasia was made. She was treated by resecting the distal 10 cm. of esophagus and anastomosing the esophagus to the stomach.

Repeated roentgenographic examinations of the esophagus during the subsequent 5 years were interpreted as achalasia without other complicating diseases. Hospitalization was necessary because of repeated pulmonary infections which finally resulted in death. At autopsy an unsuspected large carcinoma of the mid-esophagus was found.

Case vi. S.A. (144-45-88), a 68 year old male, had had known achalasia for 25 years associated with recurrent pneumonia and minimal dysphagia. Esophagoscopy revealed a 3.5 cm. diameter, circumferential ulcerated mass in the

Table II

HIATUS HERNIA AND ESOPHAGEAL CANCER

	Age	Sex	Known Duration of Hiatus Hernia	Site of Tumor	Histologic Type	Comments
1. W.McC. (103-85-05)	60	M	10 years	Distal esophagus	Adenocarcinoma	Columnar epithelium in esophagus proximal to tumor
2. W.B. (149-51-06)	76	M	?	Esophagus and stomach	Anaplastic adenocarcinoma	
3. G.G. (154-53-37)	53	M	11 years	Esophagus and stomach	Undifferentiated carcinoma	Tumor involved 5 cm. of distal esophagus and 1 cm. of stomach
4. T.L. (154-76-08)	71	F	2 months	Stomach	Hodgkin's disease	
5. I.T. (79-24-61)	65	F	12 years	Stomach, pars media but chiefly above diaphragm	Anaplastic adenocarcinoma	Hiatus hernia asymptomatic for 12 years
6. S.S. (86-52-84)	68	F	—	Stomach, below diaphragm but extending to cardia	Poorly differentiated adenocarcinoma	Probably an incidental association
7. J.C. (155-09-72)	72	M	?	Distal esophagus and stomach	Adenocarcinoma	Stomach not visualized by esophagoscopy
8. E.C. (79-07-43)	76	F	?	Stomach	Adenocarcinoma	Diagnosis missed on the initial examination
9. M.L. (76-57-70)	62	F	1 month	Distal esophagus	Adenocarcinoma	
10. M.M. (98-36-70)	62	F	several months	Distal esophagus	Squamous cell carcinoma	Hernia found at time of surgery too stenosed to permit roentgen-ray diagnosis of hernia
11. B.G. (137-77-67)	74	F	15 years	Fundus involving cardia	Adenocarcinoma	
12. J.Z. (86-07-09)	47	M	?	Distal esophagus	Adenocarcinoma	Gastric epithelium at 34 cm.
13. W.K. (134-33-80)	77	M	4 years	Distal esophagus	Squamous cell carcinoma	
14. W.R. (134-96-52)	56	M	?	Distal esophagus	Squamous cell carcinoma	
15. G.G. (16-62-58)	66	M	?	Gastric fundus	Undifferentiated carcinoma	
16. E.J. (47-93-26)	74	M	13 months	Gastric fundus	Undifferentiated carcinoma	
17. M.C. (86-21-29)	64	F	?	Distal esophagus	Undifferentiated carcinoma	
18. B.R. (17-46-82)	63	M	?	Gastric fundus	Adenocarcinoma	

mid-esophagus which proved to be an epidermoid carcinoma. Roentgenograms disclosed a large esophagus, with disproportionately greater dilatation of the proximal one-third. The multiple filling defects were interpreted as retained food particles and not even in retrospect could the tumor be identified (Fig. 9).

HIATUS HERNIA AND ESOPHAGEAL CANCER

Herniation of a portion of stomach through the esophageal hiatus is such a common condition that it would be surprising, if at times, this did not occur in association with cancer of the stomach or esophagus. In 1949, Brick[8] claimed that the chance of a patient with a hiatus hernia developing a gastric cancer was four times less than in patients without a hiatus hernia. Smithers,[42] on the other hand, after analyzing 155 cases, concluded that there was an established association between hiatus herniation and cancer of the esophagus.

A review of the carcinomas of the esophagus and stomach at the Columbia-Presbyterian Medical Center for the past 7 years disclosed 18 patients in whom a hiatus hernia was associated with either a cancer of the stomach or esophagus (Table II). This material can be subdivided into 4 groups: (1) cancer limited to the nonherniated portion of stomach (1 patient); (2) cancer limited largely to the herniated portion of stomach (4 patients); (3) epidermoid carcinomas of distal esophagus and hiatus hernia (2 patients); and (4) hiatus hernia associated with adenocarcinoma of the gastric cardia or distal esophagus (11 patients).

ROENTGEN APPEARANCE

The roentgen appearance of these lesions was varied but the diagnostic accuracy was surprisingly low. In 6 patients with gross fungating masses, the roentgen diagnoses were obvious. In 2 patients a gastric narrowing was erroneously considered to be entirely due to the constricting effect of the hiatus and insufficient attention was directed to minor irregularities of contours and peculiar mucosal patterns (Fig. 10, *A* and *B*). Two other patients with rather large fundal masses were diagnostic problems largely because of the abnormal anatomic relationships in the herniated portion of stomach (Fig. 11). When the lower esophageal stenosis was extreme, insufficient filling of the lumen distal to the obstruction made it impossible to recognize the presence of an associated hiatus hernia. Large rugae, a common normal variant in the fundus, are particularly difficult to recognize as a manifestation of neoplasm when they occur in the herniated portion of stomach (Fig. 5, *A* and

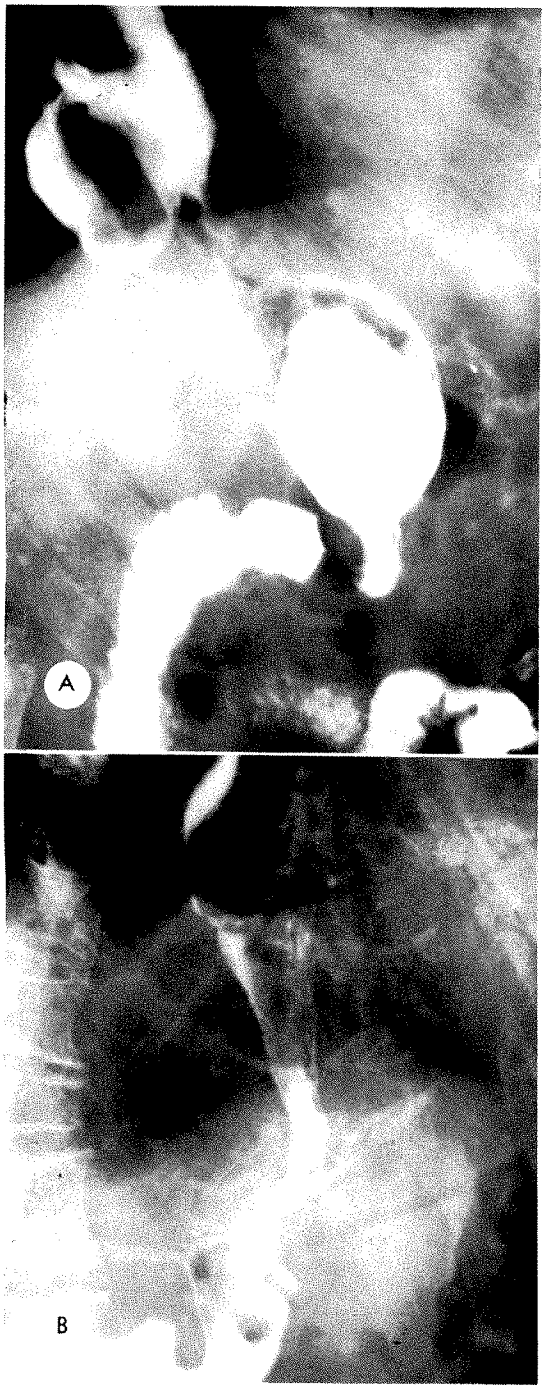


Fig. 10. E.C. (79-07-43). Large hiatus hernia in a 76 year old female. (*A*) The significance of the irregularity and lack of distensibility of the narrowed segment of stomach was not fully appreciated and attributed to the constricting influence of the hiatus. (*B*) Six months later almost the entire stomach was involved by an infiltrating cancer.

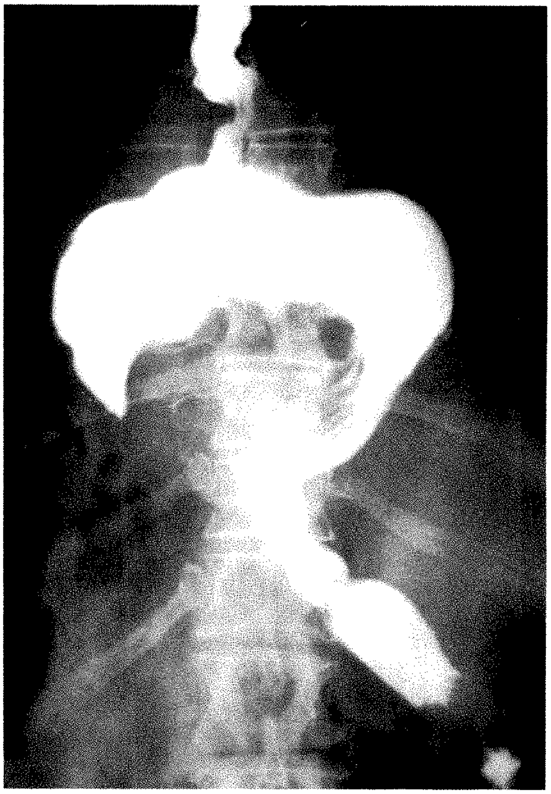


Fig. 11. T.L. (154-76-08). Large tumor (Hodgkin's disease) involving the lesser curvature aspect of the herniated portion of stomach. This is a diagnostic problem only because of the abnormal anatomic relationships.

B). Careful attention must be given to asymmetric flattening of the distal esophagus which constituted the major diagnostic clue in 2 instances (Fig. 12 and 13, *A* and *B*). The most difficult diagnosis is the differentiation between hiatus hernia associated with peptic esophagitis and hiatus hernia associated with a constricting neoplasm (Fig. 14). Statistically the former is more frequent.

Diagnostic errors may be minimized if meticulous roentgenographic techniques are used. This should include roentgenograms of the fully distended and partially filled esophagus in at least two projections. Complete distention is best and most consistently obtained by having the patient drink barium through a tube while lying prone on an abdominal compression device.

The true incidence of this association is difficult to accurately assess since diagnosis of hiatus hernia partly depends upon the

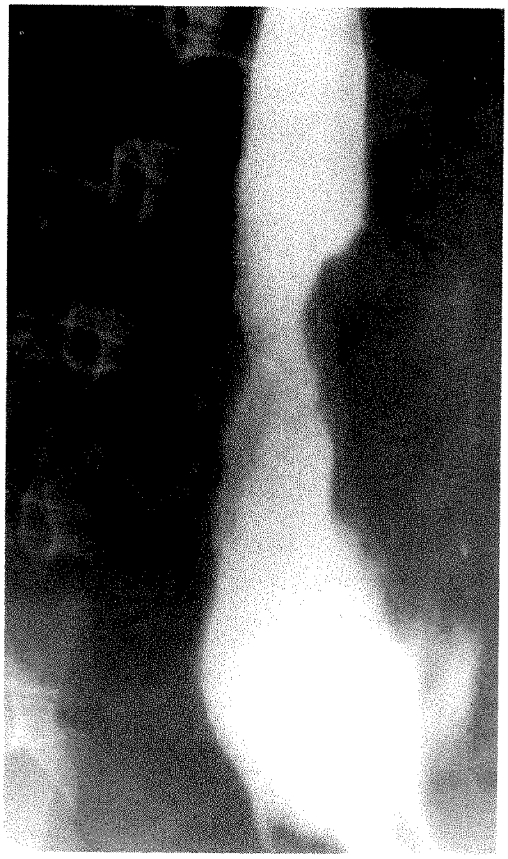


Fig. 12. G.G. (154-53-37). A 53 year old male with an 11 year history of hiatus hernia and anterior chest pain after swallowing of 2 months' duration. Note the extensive area of flattening and rigidity in the distal esophagus. At surgery an extensive infiltrative anaplastic carcinoma was found.

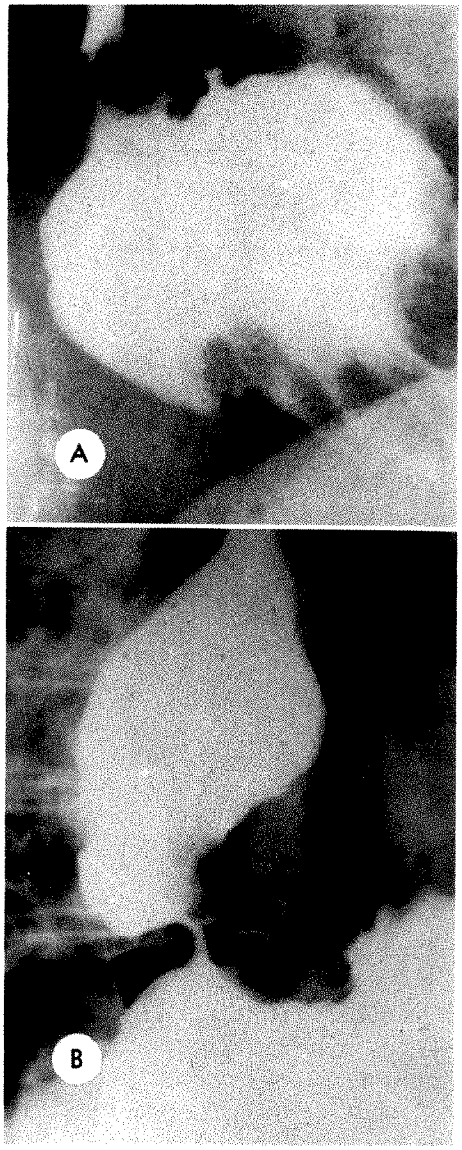


Fig. 13. W. McC. (103-85-05). A 60 year old male with dysphagia of one months' duration and hiatus hernia of 10 years' duration. (*A*) Initial demonstration of hiatus hernia. (*B*) Development of cancer 10 years later. The presence of tumor was manifested by asymmetry and flattening of the distal esophagus.

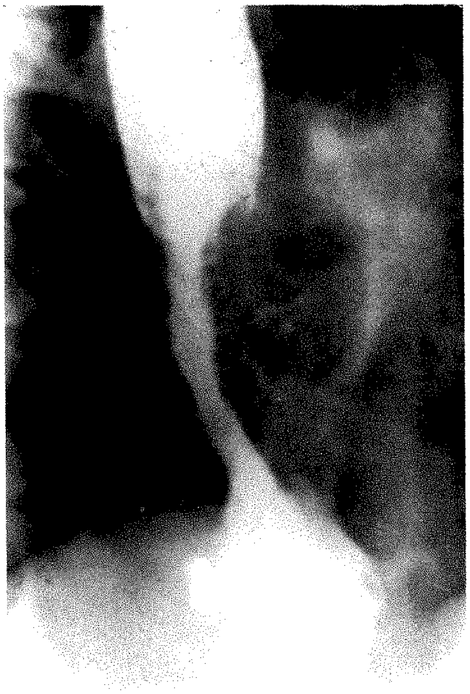


FIG. 14. J.Z. (86-07-09). A 47 year old male with a 7 month history of substernal pain. Acute onset of dysphagia 3 days before this roentgenogram was interpreted as peptic esophagitis and hiatus hernia. A biopsy of a granular excrescence surrounding an ulcer at 34 cm. showed only gastric mucosa. At exploration a hiatus hernia and adenocarcinoma of the esophagogastric junction were found.

roentgenologic technique utilized and the diagnostic criteria accepted. For example, Sommer and Stevenson[44] have demonstrated that 93 per cent of small hiatus hernias would be missed if only erect fluoroscopy were utilized. In addition, a previously existing small hiatus hernia may be no longer recognizable because of the effect of the neoplasm (Fig. 5, *A* and *B*).

McConchie[31] reported that 8 per cent of 60 patients whose symptoms associated with the hiatus hernia warranted operation had an associated carcinoma in the herniated portion of stomach or in the esophagus just above. Kay and Cross,[25] from their series of over 200 patients with esophageal cancer containing 7 patients with associated hiatus hernia, extrapolated an incidence of 3,500 per 100,000 population, and concluded that this was obviously higher than in the general population.

Stemmer and Adams[46] pointed out that in their series the incidence of gastric carcinoma in patients with hiatus hernia was about the same as in patients with symptoms of indigestion without hiatus hernia. However, in their series of patients with a congenital short esophagus, the incidence of carcinoma was 24 per cent (8 of 33). Resano *et al.*[39] report carcinoma complicating 20 of 54 (37 per cent) cases of congenital short esophagus and 15 of 102 (14 per cent) cases of acquired short esophagus.

The congenital short esophagus in contrast to the acquired short esophagus is not a form of hiatus hernia, although it may be associated with it. Barrett,[5] on the basis of the normal anatomic relation of the gullet and stomach with special reference to the vascular supply and ligamentous attachments, holds that most cases of so-called congenital short esophagus with partial thoracic stomach are examples of an otherwise normal esophagus, the lower portion of which is lined by columnar epithelium. This entity has been referred to as the Barrett esophagus.

This columnar epithelium forms simple tubular glands confined to the mucosa and produces a mucus secretion containing no digestive juices. The finding of esophageal mucus glands in the submucosa deep to the columnar epithelium as reported by Allison and Johnstone[2] and Azzopardi and Menzies[4] seems to substantiate their belief that this organ represents esophagus rather than stomach. According to Hayward[21] the distal 2 cm. of esophagus plus a slight extension into the stomach, is normally lined by the type of mucosa which he terms junctional epithelium and regards as esophageal. In Hayward's opinion, the columnar epithelium found in the Barrett esophagus is identical with junctional epithelium. Although both Smithers and Barrett regard this anomaly as due to an embryologic failure of conversion of the columnar epithelium to a squamous type, it has been suggested by Azzopardi and Menzies,[4] Goldman and Beckman,[19] Dodge,[13] and Hayward[21] that this anomaly may be acquired due to gastric reflux, ulceration and healing of the eroded surface by regeneration of columnar epithelium from below.

Smithers[42] has pointed out that, although the majority of esophageal tumors associated with hiatus hernias might be expected to be squamous cell tumors since these constitute 90 per cent of esophageal tumors, 36 per cent were adenocarcinomas. He suggested that this might be a special developmental tendency when the lower esophagus is lined by gastric mucosa. Other, more recent reports also seem to indicate a tendency to malignant transformation in this form of esophagus. At times, the presence of an esophagus lined by columnar epithelium may be suspected from the roentgenographic appearance. This characteristic picture, according to Allison and Johnstone[2] is that of a stenosis, usually at the level of the aortic arch, followed by a segment wider than the normal esophagus and then a pouch of herniated stomach (Fig. 15).

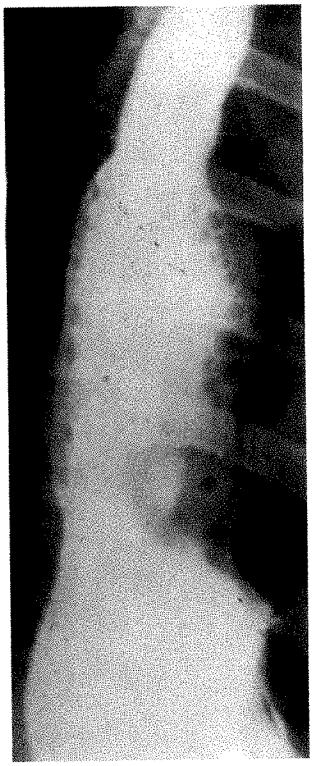


Fig. 15. S.M. (23-46-95). Roentgenographic appearance of the Barrett esophagus. Note small hiatus hernia and dilated lumen up to the level of the aortic arch. Multiple biopsies verified the presence of columnar epithelium extending to the level of the aortic arch.

SUMMARY

1. The problems of differential diagnosis in the lower esophagus resulting from the similarities and associations of carcinoma with achalasia and hiatus hernia have been discussed.

2. The available evidence suggests that cancer is more frequent in the esophagus involved by achalasia and this may also be true for some types of hiatus hernia.

William B. Seaman, M.D.
Department of Radiology
Columbia University
New York, New York

Grateful acknowledgement is made to Dr. Richmond Moore for permission to include Case VI.

REFERENCES

1. Adler, R. H., and Rodriguez, J. Association of hiatus hernia and gastroesophageal malignancy. *J. Thoracic Surg.*, 1959, *37*, 553–569.
2. Allison, P. R., and Johnstone, A. S. Oesophagus lined with gastric mucous membrane. *Thorax*, 1953, *8*, 87–90.
3. Asherson, N. Cardiospasm: intermittent; initial manifestation of carcinoma of cardia. *Brit. J. Tuberc.*, 1952, *47*, 39–40.
4. Azzopardi, J. G., and Menzies, T. Primary oesophageal adenocarcinoma. *Brit. J. Surg.*, 1962, *49*, 497–506.
5. Barrett, N. R. In: Modern Trends in Gastroenterology. Second series. Edited by Jones, F. A. Paul B. Hoeber, New York, 1958.
6. Barrett, N. R. Benign stricture of lower oesophagus. *Proc. Roy. Soc. Med.*, 1960, *53*, 399–402.
7. Barrett, N. R. Lower esophagus lined by columnar epithelium. *Surgery*, 1957, *41*, 881–894.
8. Brick, I. B. Hiatus hernia and carcinoma of stomach and esophagus. *Gastroenterology*, 1949, *13*, 47–56.
9. Brombart, M. Clinical Radiology of the Oesophagus. John Wright & Sons, Bristol, 1961.
10. Camara-Lopes, L. H. Carcinoma of esophagus as complication of megaesophagus; analysis of seven cases. *Am. J. Digest. Dis.*, 1961, *6*, 742–756.

11. Code, C. F., Creamer, B., Schlegel, J. F., Olsen, A. M., Donoghue, F. E., and Andersen, H. A. An Atlas of Esophageal Motility in Health and Disease. Charles C Thomas, Publisher, Springfield, Ill., 1960.
12. Debray, C., Besancon, F., and Janin, B. Diagnosis of "essential hypertension of cardia"; similar electromanographic syndrome in 4 cases of cancer. *Semaine hôp. Paris*, 1962, *38*, 1565–1568.
13. Dodge, O. G. Gastro-oesophageal carcinoma of mixed histological type. *J. Path. & Bact.*, 1961, *81*, 459–471.
14. Dodge, O. G. Intraoesophageal adenocarcinoma. *Gut*, 1960, *1*, 351–356.
15. Ellis, F. G. Natural history of achalasia of cardia. *Proc. Roy. Soc. Med.*, 1960, *53*, 663–666.
16. Feldman, M., and Myers, P. Coexistence of carcinoma of stomach and esophageal hiatus gastric hernia. *Am. J. M. Sc.*, 1952, *224*, 519–521.
17. Friedman, A. I. Carcinoma of stomach in association with hiatus hernia. *Ann. Int. Med.*, 1957, *47*, 812–817.
18. Giraud, M., and Beraud, S. Les signes radiologiques des néoplasmes juxta-cardiaques de l'estomac à manifestations cliniques pseudo-oesophagiennes. *J. de radiol. et d'électrol.*, 1947, *28*, 58–62.
19. Goldman, M. C., and Beckman, R. C. Barrett syndrome; case report with discussion about concept of pathogenesis. *Gastroenterology*, 1960, *39*, 104–110.
20. Gore, I., and Lam, C. R. Carcinoma of esophagus complicating cardiospasm; report of case. *J. Thoracic Surg.*, 1952, *24*, 43–49.
21. Hayward, J. Lower end of oesophagus. *Thorax*, 1961, *16*, 36–41.
22. Hellemans, N., and Julius, J. Combination of carcinoma in cardial region of stomach with diaphragmatic hiatal hernia. *Nederl. tijidschr. geneesk.*, 1961, *105*, 2534–2538.
23. Hoover, W. B. Carcinoma associated with esophageal diverticulum; report of case. *S. Clin. North America*, 1945, *25*, 707–712.
24. Kay, E. B. Inferior esophageal constrictor in relation to lower esophageal disease. *J. Thoracic Surg.*, 1953, *25*, 1–15.
25. Kay, E. B., and Cross, F. S. Chronic esophagitis; possible factor in production of carcinoma of esophagus. *A.M.A. Arch. Int. Med.*, 1956, *98*, 475–481.
26. Lawrence, K., and Shoesmith, J. H. Review of treatment of cardiospasm. *Thorax*, 1959, *14*, 211–215.
27. le Roux, B. T. Analysis of 700 cases of carcinoma of hypopharynx, oesophagus, and proximal stomach. *Thorax*, 1961, *16*, 226–255
28. Marshak, R. H. Roentgen findings of benign and malignant tumors of esophagus. *J. Mt. Sinai Hosp.*, 1956, *23*, 75–89.
29. Marshak, R. H., and Eliasoph, J. Cardiospasm or carcinoma? *Am. J. Digest. Dis.*, 1957, *2*, 11–25.
30. Mathews, E. C., and Vinson, P. P. Carcinoma of esophagus complicating cardiospasm; report of case. *Gastroenterology*, 1950, *15*, 747–753.
31. McConchie, I. Gastro-oesophageal carcinoma in hiatal hernia. *Australian & New Zealand J. Surg.*, 1961, *31*, 6–11.
32. Miller, C. Carcinoma of thoracic oesophagus and cardia; review of 405 cases. *Brit. J. Surg.*, 1962, *49*, 507–522.
33. Mueller, B., and Corajod, E. Case of gastric cancer of endothoracic stomach caused by diaphragmatic hernia; total gastrectomy. *Arch. mal. app. digest.*, 1961, *50*, 241–244.
34. Pack, G. T., Butler, F. S., and Katz, E. Development of cancer in dystopic and ectopic thoracic stomachs; report of two cases. *J. Thoracic Surg.*, 1952, *23*, 593–601.
35. Pattinson, J. N., Osborne, G., and Morson, B. C. Hiatus hernia with adenocarcinoma arising in region of cardia. *J. Fac. Radiologists*, 1955, *7*, 90–101.
36. Peters, P. M. Congenital short oesophagus. *Thorax*, 1958, *13*, 1–11.
37. Peyman, M. A. Achalasia of cardia, carcinoma of oesophagus, and hypertrophic pulmonary osteoarthropathy. *Brit. M. J.*, 1959, *1*, 23–25.
38. Potter, S. E., Rasmussen, J. A., and Best, R. R. Problem of carcinoma in achalasia. *J. Thoracic Surg.*, 1956, *31*, 543–549.
39. Resano, H., Malenchini, M., Barani, J. C., and Barg, S. Oesophage court et cancer. *Ann. oto-laryng.*, 1957, *74*, 150–154.
40. Santy, P., Michaud, P., and Viard, H. Cancer sur megaoesophage. *Lyon chir.*, 1958, *54*, 354–367.
41. Smith, R. A. Cancer in thoracic stomach. *J. Thoracic Surg.*, 1955, *29*, 568–571.
42. Smithers, D. W. Association of cancer of stomach and oesophagus with herniation at oesophageal hiatus of diaphragm. *Brit. J. Radiol.*, 1955, *28*, 554–564.
43. Smithers, D. W. Adenocarcinoma of oesophagus. *Thorax*, 1956, *11*, 257–267.
44. Sommer, A. W., and Stevenson, C. L. Hiatal hernia; evaluation of diagnostic procedures. *Am. J. Digest. Dis.*, 1961, *6*, 412–422.
45. Sparks, J. V. Some post-operative findings in hiatus hernia. *J. Fac. Radiologists*, 1958, *9*, 84–89.
46. Stemmer, E. A., and Adams, W. E. Incidence of

carcinoma at esophagogastric junction in short esophagus. *Arch. Surg.*, 1960, *81*, 771–780.

47. STOUT, A. P. Atlas of Tumor Pathology, Sect. V, Fasc. 20. Tumors of the Esophagus. Armed Forces Institute of Pathology, Washington, D. C., 1957.
48. TANNER, N. C. Treatment of oesophageal hiatus hernia. *Lancet*, 1955, *2*, 1050–1055.
49. TANNER, N. C., and SMITHERS, D. W., Editors. Tumours of the Esophagus. E. & S. Livingstone, Edinburgh, 1961.
50. VIRNO, F., and CARBONI, R. Association of cancer of esophagus with "so-called cardiospasm" in review of literature with presentation of personal case. *Arch. chir. torace*, 1959, *13*, 499–521.
51. WILEY, A. M. Carcinoma in hiatus herniae. *Postgrad. M. J.*, 1956, *32*, 259–261.

* * *

RETROTRACHEAL LYMPHADENOPATHY IN BRONCHIAL CARCINOMA, REVEALED BY THE BARIUM-FILLED ESOPHAGUS*

By FELIX G. FLEISCHNER, M.D., *and* ECKART SACHSSE, M.D.
BOSTON, MASSACHUSETTS

THE roentgen examination of the posterior mediastinum is substantially aided by the barium-filled esophagus. This pertains also to mediastinal lymphadenopathy. The paratracheal, tracheobronchial and hilar lymph nodes become visible immediately, when they are sufficiently enlarged, by projection beyond the normal contours of the supracardiac mediastinal shadow. They may also impinge upon the air space of the trachea or main bronchi, best seen on a high penetration roentgenogram or laminagram. Contrarily, the bifurcation lymph nodes, also called carinal or subcarinal lymph nodes, are not directly visible. The esophagus passes the carina slightly to the left of the midline and is closely attached to the trachea and left main bronchus. Therefore, enlargement of the bifurcation lymph nodes of both inflammatory or neoplastic nature is readily recognized by displacement of the barium-filled esophagus to the left and posteriorly. Enlargement of these lymph nodes is especially characteristic of bronchial carcinoma and its demonstration in association with a chronic pulmonary consolidation is highly suggestive of this diagnosis.[1,3,4]

The present study concerns metastatic involvement of another group of mediastinal lymph nodes, little known previously.[1,4,6] Rouvière[8] described a lymph node of small size behind the inferior part of the trachea in the path of lymphatic vessels which connect the bifurcation lymph nodes with the right paratracheal chain. This was present in about 1 out of 8 cases.

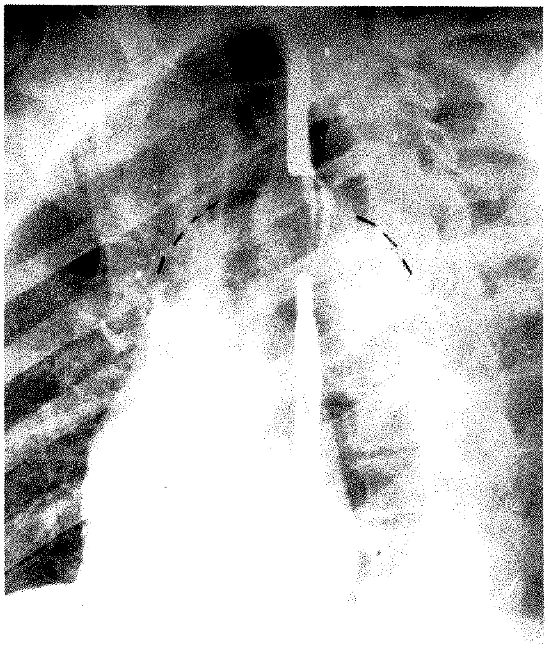


FIG. 1. Case 1. Left anterior oblique view with barium filled esophagus. The aortic arch is indicated by the interrupted black line. An ovoid soft tissue mass lies between the air column of the lower trachea and the esophagus, compressing and displacing both.

REPORT OF CASES

CASE 1. H.N., a male of 45 years, had been hoarse for less than 2 weeks. A slight irregular increase of the left hilar shadow was noted. The left vocal cord was paralyzed but there was no phrenic paralysis. The barium-filled esophagus showed a round soft tissue mass between the esophagus and the lower trachea, about 4 cm. in length and 3 cm. in width, best seen in the oblique views (Fig. 1 and 2, *A* and *B*).

Bronchograms were interpreted as negative. In retrospect, a slight irregularity of the upper wall of the left main bronchus at its trifurcation was recognized on them. Bronchoscopy was technically impossible. No cancer cells were found in the sputum. The tentative diagnosis was a malignant lesion of unknown origin with

---

* From the Departments of Radiology, Peter Bent Brigham Hospital and Harvard Medical School, Boston, Massachusetts.

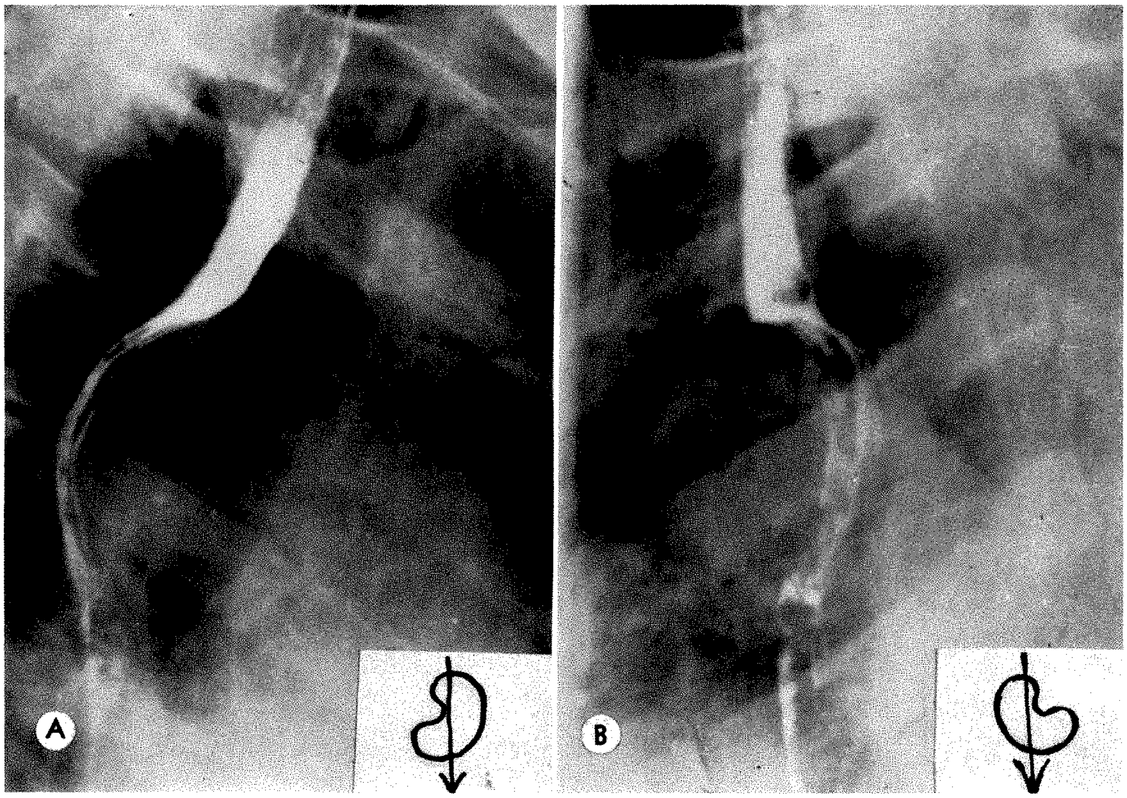


FIG. 2. Case I. (*A* and *B*) Spot roentgenograms in the right and left anterior oblique views.

mediastinal extension, or an independent benign mediastinal lesion, a leiomyoma of the esophagus or a vascular anomaly. In the following 7 weeks, increasing dysphagia developed. On an exploratory left thoracotomy, a small tumor mass was found in the depth of the interlobar fissure between the upper and lower lobe, connected with both lobes. Numerous tumorous lymph nodes were seen at the hilus and in the mediastinum. The lesion between the esophagus and trachea was also identified as a lymph node. Only a biopsy was performed which was reported as squamous cell carcinoma.

A follow-up roentgen examination showed that the lymphonodular mass had broken down and opened into the esophagus (Fig. 3). Some time later an opening into the trachea was also noted so that barium passed from the esophagus through the tumor cavity into the trachea (Fig. 4). Supervoltage therapy and nitrogen mustard did not arrest the rapid downhill course and the patient died 7 months after the onset of symptoms.

On autopsy extensive coalescent mediastinal tumor masses were found and also the tumor fistula between the trachea and esophagus was confirmed. No residual tumor was found in the left lung after radiation teratment.

Comment. A bronchial carcinoma caused early mediastinal symptoms, hoarseness and dysphagia at a time when the routine chest roentgenograms showed only minimal questionable changes about the left hilus. But even at that "early" stage, the mediastinal spread was revealed by the enlarged retrotracheal lymph node identified with the barium-filled esophagus. Tumor necrosis in this lymph node led to a tumorous esophagotracheal fistula.

CASE II. E.R., a male of 73 years, was first seen for increasing dyspnea, cough, and weight loss. The chest roentgenogram showed a consolidation in the lower medial portion of the right upper lobe, a small pleural effusion on the right and marked pulmonary emphysema. There was no diaphragmatic paralysis. While no enlarged bifurcation lymph nodes could be identified with the barium-filled esophagus, a soft tissue

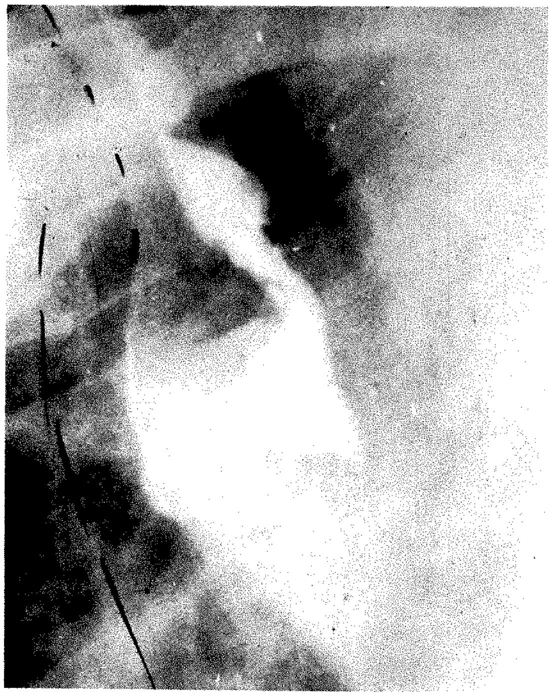


FIG. 3. Case I. Left anterior oblique view at a later stage. The lymphonodular tumor had broken down to form an abscess, widely communicating with the esophagus, as outlined by barium entering from the esophagus.

mass was seen embedded between the trachea and the esophagus, just above the aortic arch (Fig. 5). Since carcinoma cells were found in the pleural fluid, the diagnosis of bronchial carcinoma was established and inoperability was assumed from the mediastinal lymphadenopathy. Later, skeletal and pulmonary metastases appeared and treatment with nitrogen mustard seemed to provide temporary relief.

Comment. The observation of an enlarged retrotracheal lymph node brought into relief by the barium-filled esophagus helped to establish the diagnosis of bronchial carcinoma and its inoperability.

CASE III. A.D., a male of 74 years, had hoarseness for 8 weeks and slight dysphagia. He was a heavy smoker and had lost 20 lb. in recent months. On examination, a left vocal cord paralysis and also absence of the gag reflex were found. The roentgen examination showed a soft tissue mass in the region of, and apparently closely connected with, the aortic arch. It did not seem to pulsate. The barium-filled esophagus revealed an oblong soft tissue mass between the lower trachea and the esophagus (Fig. 6).

Esophagoscopy was negative. On bronchoscopy, the left main bronchus was found to be angulated by a pulsatile mass. During left cervical mediastinal exploration, a pulsatile mass was found over the posterior aortic arch and a scalene fat pad was excised. In this fat pad 5 lymph nodes were identified and were reported as metastatic undifferentiated carcinoma.

Comment. This elderly man with a left upper mediastinal and paramediastinal mass had evidence of a lesion in the upper left mediastinum manifested by left vocal cord paralysis and disturbance of the swallowing act with aspiration into the trachea. While the general roentgenologic appearance was ambivalent between tumor and aortic aneurysm, the discovery of an enlarged retrotracheal lymph node pointed strongly to bronchial carcinoma. Nevertheless, the impression of transmitted pulsation observed by the bronchoscopist and even at the mediastinal exploration was so strong that

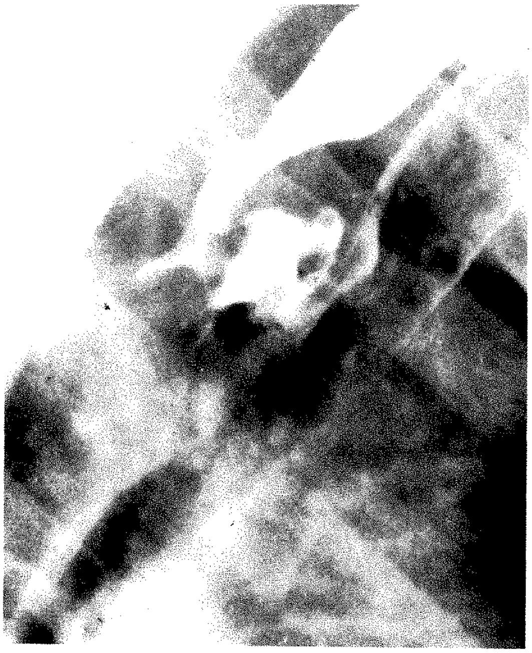


FIG. 4. Case I. Right lateral view. The barium enters from the esophagus (left) and passes through the tumor abscess into the trachea (right), thus outlining the tumorous esophagotracheal fistula.

the surgeon believed it to be an aneurysm. The pathologist's finding of metastatic lesions in the removed lymph nodes proved bronchial carcinoma.

CASE IV. R.D., a 64 year old male, was a heavy cigarette smoker and had had a chronic cough for many years. During the previous 2 months, he had dull chest pain and increasing dysphagia. On examination only emphysema and chronic bronchitis were found. The roentgen examination showed a prominent right hilar shadow (Fig. 7). The esophagus was markedly narrowed at the level of the aortic arch and apparently rigidly surrounded by firm masses, most marked at its right anterior aspect (Fig. 8*A*). An oblong soft tissue mass separated the esophagus from the trachea as seen in the left anterior oblique view (Fig. 8*B*). Slight displacement of the esophagus at a lower level suggested also enlargement of the bifurcation lymph nodes. On esophagoscopy, a mass was seen compressing the wall but without mucosal destruction. It felt stony hard to touch with the esophagoscope. Neither from the esophagus, nor by means of bronchoscopy which did not elucidate the situation, was representative diagnostic material (carcinoma cells) obtained. A left thoracotomy was performed. Only when the mediastinum was entered were large tumor masses encountered adherent to the vertebral bodies, encircling the aortic arch and the esophagus, with broad extension to the membranous wall of the trachea. These tumor masses were found to be contiguous with lymphonodular masses in the hilar region of the right lung. The biopsy specimen taken from a mediastinal lymph node was reported as poorly differentiated epidermoid carcinoma. The patient succumbed to a postoperative *Staphylococcus* infection. Autopsy was not obtained.

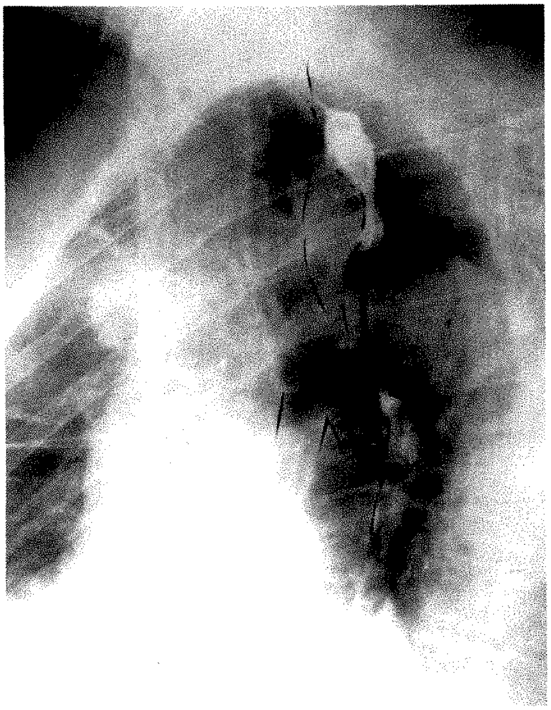


FIG. 5. Case II. Left anterior oblique view. The trachea and the barium-filled esophagus are partly outlined by interrupted black lines. A spindle-shaped lymphonodular soft tissue mass lies between the trachea and esophagus, compressing both, above the level of the aortic arch.

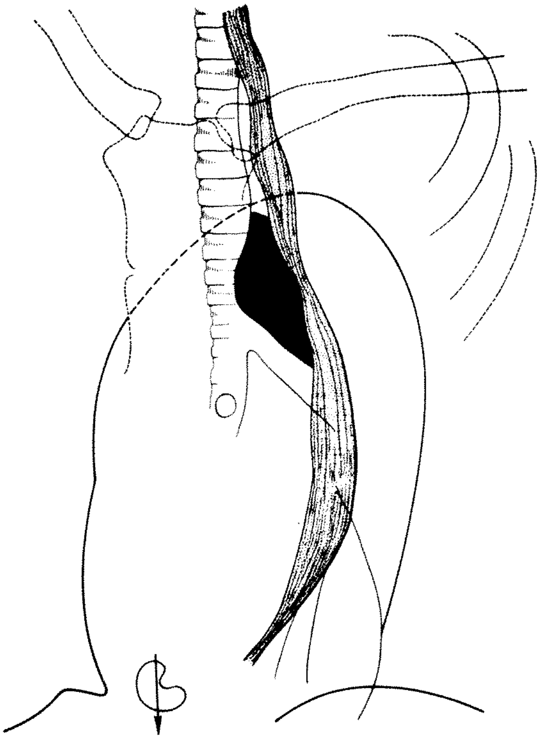


FIG. 6. Case III. Tracing of a roentgenogram in the left anterior oblique view showing an oblong mass between the trachea and barium-filled esophagus, compressing both.

Comment. The routine chest roentgenograms showed only questionable slight changes at the right hilus. Dysphagia, the presenting symptom, led to an immediate examination of the esophagus. A rigid enveloping lesion was found at the level of the

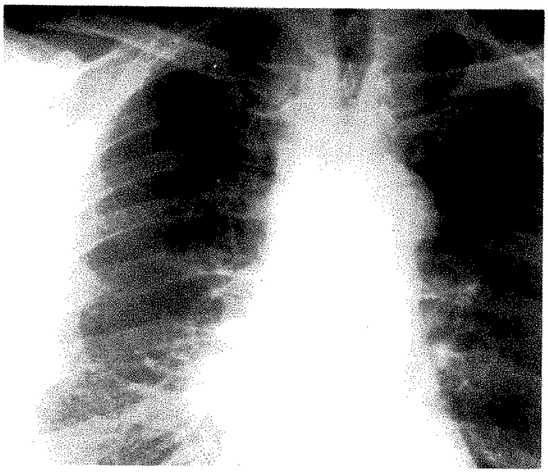


FIG. 7. Case IV. Posteroanterior view showing the enlarged right hilar shadow.

aortic arch and, in addition, lymphonodular masses between the trachea and the esophagus and at the bifurcation were noted. Esophagoscopy and bronchoscopy partly confirmed these findings with the addition that no origin from the mucosa of the esophagus and bronchi could be identified. The lateralizing evidence was so unobtrusive that because of the surgical impression of a primary mediastinal tumor exploratory thoracotomy was undertaken on what turned out to be the wrong side. Extensive metastatic lymphonodular tumor masses made the lesion non-resectable.

DISCUSSION

The success of the thoracic surgeon in combatting bronchial carcinoma is often dampened by the frequent encounter of direct or metastatic extension of the tumor into the mediastinum. In the detection of mediastinal involvement, the plain roentgenogram demonstrating paratracheal lymph nodes, mediastinal venography, and, more recently, costal bone marrow venography have been of considerable value. These roentgenologic endeavors were paralleled by surgical excision of prescalene lymph nodes and cervical mediastinal exploration.

In the program of eliminating unsuitable cases from surgical treatment, the exploration of the posterior mediastinum by roentgen study of the esophagus is simple and reliable in the detection of enlarged carinal lymph nodes.

The close topographic relationship of some lymph nodes to the esophagus is well known. Patients with advanced bronchial carcinoma often have dysphagia, which is an early symptom in rather frequent cases, and the presenting symptom in rarer instances. As a matter of fact, this is sometimes the reason which first leads the patient to his physician. Sometimes a primary carcinoma of the esophagus may be suspected even roentgenologically. Only the fact that the stricture is found at the level of the bifurcation lymph nodes and that it is not circumferential cautions one to consider the possibility that it may be caused by pressure, adhesion or invasion from tumorous lymph nodes. Also, the pathologists are familiar with instances which, at first

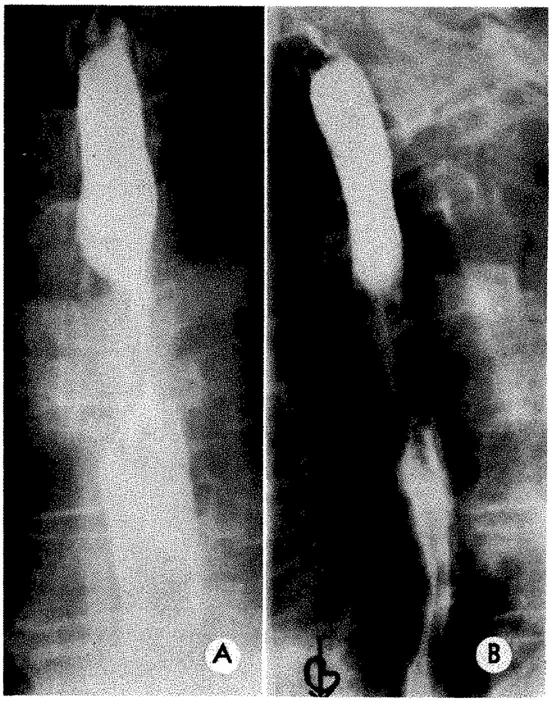


FIG. 8. Case IV. (*A*) Posteroanterior view showing the esophagus compressed at the level of the aortic arch. (*B*) Left anterior oblique view. The trachea and esophagus are separated from each other by an oblong soft tissue mass. The trachea and carina are indicated by interrupted lines.

glance, resemble an esophageal carcinoma. The discovery of a pulmonary tumor or the histology of adenocarcinoma leads to the proper diagnosis of primary bronchial carcinoma with mediastinal metastases and esophageal invasion.

In numerous instances metastatic mediastinal lymphadenopathy indicates inoperability of the bronchial carcinoma. This is particularly true for the paratracheal and bifurcation lymph nodes. The paratracheal lymph nodes, if sufficiently enlarged, widen the upper mediastinal shadow; they themselves and the widened vena cava or anonymous vein increase the soft tissue shadow between the trachea and the clear lung field. The enlarged bifurcation lymph nodes are brought into relief by the barium-filled esophagus best seen in left anterior oblique roentgenograms. The gross involvement of these lymph nodes almost always indicates inoperability. In Gladnikoff's[4] diagram the roentgen-visible involvement of the mediastinal lymph nodes in 98 cases of bronchial carcinoma is indicated with figures specifying the frequency of involvement in his series (Fig. 9). The topmost lymph node, properly called supraarcuar lymph node, was affected 3 times; the lymph node to the left of and above the bifurcation and extending behind the trachea (the retrotracheal lymph node) was affected 9 times. The involvement of hilar lymph nodes marked by 17 and 52 on the right and by 15 and 25 on the left, as well as the lymph nodes in the lower mediastinum and ligamentum pulmonale (3 and 8) is still consistent with operability in a fair number of cases. Involvement of the supraarcuar, retrotracheal and bifurcation lymph nodes, contrarily, is associated with a forbiddingly low operability. It is well known that the upper medial parts of the left upper lobe, segments 1, 2 and 3, and to a lesser degree also of the right upper lobe, segments 1 and 2, usually drain via upper hilar lymph nodes to the paratracheal lymphatics, thus bypassing the bifurcation lymph nodes, while the bifurcation lymph nodes represent an almost obligatory sump for the lymphatic drainage of the remainder of the lungs.

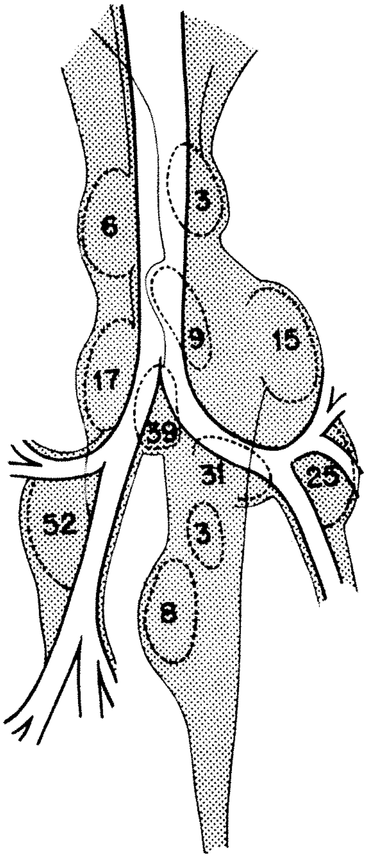


Fig. 9. Schematic diagram of the distribution of the mediastinal lymph nodes and the relative frequency of metastases in them, in a series of 98 cases of bronchial carcinoma, according to Gladnikoff. (Reproduced with permission of *Acta radiol.*[4])

The first case of the series presented here corresponds to the metastatic enlargement of the supraarcuar lymph node, while the other cases show involvement of the lower lymph node with extension behind the trachea: the retrotracheal lymph node. In both situations these enlarged lymph nodes are intimately connected with the aortic arch and may cause difficulty in the distinction from an aortic aneurysm; this was true in our Case III. It is well known that transmitted pulsation often cannot be distinguished from endogenous expansile pulsation by fluoroscopy, electrokymography and even by direct surgical inspection, as in Case III.

The differential diagnosis includes any kind of primary or metastatic tumor in or close to the upper mediastinum, carcinoma, sarcoma or malignant lymphoma.

Similar encroaching masses may originate from a substernal goiter extending retrotracheally or an ectopic parathyroid adenoma. Left sided vocal cord paralysis and hoarseness always focus attention on this area.

In all 4 cases of our observation the primary carcinoma was in the upper lobe; in Cases I and III in the left, and in Cases II and IV in the right upper lobe. The primary tumor was always in the most medial, paramediastinal part of the lobe. Only in Case IV could enlargement of the bifurcation lymph nodes be identified roentgenologically. In some of these instances, the primary tumor in the lung was either small or hardly visible on the plain roentgenogram.

SUMMARY

The value of the barium-filled esophagus as a posterior mediastinal landmark in the investigation of the size and chamber enlargement of the heart, vascular anomalies, and primary and secondary tumors is well known. Also metastatic enlargement of the bifurcation lymph nodes in the case of bronchial carcinoma can well be determined with all the diagnostic and prognostic implications. Less well known and less constant are lymph nodes between the lower trachea and esophagus. They lie in the lymphatic drainage path for the medial portion of the right upper lobe and upper three segments of the left upper lobe. In the case of carcinoma in these areas, metastatic enlargement of these retrotracheal lymph nodes may present as a round or oblong soft tissue mass embedded between the lower trachea and esophagus. Usually this is best seen in the left anterior oblique view.

Four such cases are reported and the diagnostic possibilities discussed. Enlargement of this lymph node group is often accompanied by hoarseness and dysphagia and may be an "early" roentgen sign when the primary pulmonary lesion is barely visible. Nevertheless, this metastatic involvement usually indicates extension of the disease beyond surgical control.

Felix G. Fleischner, M.D.
Peter Bent Brigham Hospital
721 Huntington Avenue
Boston 15, Massachusetts

REFERENCES

1. Bachman, A. L. Radiographic diagnosis of mediastinal involvement in carcinoma of lung. *J. Mt. Sinai Hosp.*, 1957, *24*, 4–13.
2. Bignall, J. R. Carcinoma of lung. In: Neoplastic Disease at Various Sites. Vol. I. Edited by Smithers, D. W. E. & S. Livingstone, Ltd., Edinburgh, 1958.
3. Fleischner, F. G. Esophagus and mediastinal lymphadenopathy in bronchial carcinoma. *Radiology*, 1952, *58*, 48–56.
4. Gladnikoff, H. Roentgenographic study of mediastinum in health and in primary pulmonary carcinoma. *Acta radiol.*, 1948, Suppl. 73.
5. Laustela, E. Regional lymph node metastasis in primary bronchogenic carcinoma: pathological study of 100 resected cases. *Ann. chir. et gynaec. Fenniae*, 1958, Suppl. 80, 1–39.
6. McCort, J. J., and Robbins, L. L. Roentgen diagnosis of intrathoracic lymph node metastases in carconoma of lung. *Radiology*, 1951, *57*, 339–359.
7. Nohl, H. C. Investigation into lymphatic and vascular spread of carcinoma of bronchus. *Thorax*, 1956, *11*, 172–185.
8. Rouvière, H. Anatomy of the Human Lymphatic System. Edward Brothers, Inc., Ann Arbor, Mich., 1938.

* * *

Vol. 90, No. 4

ESOPHAGEAL HIATUS HERNIA OF THE STOMACH

By JOHN A. MARTIN, M.D.
ROANOKE, VIRGINIA

MANY methods and maneuvers have been used for the roentgen study of the esophagogastric area. Among these are straight leg-raising, lowering the patient's head, the Valsalva maneuver and others.

Theoretically, a hiatus hernia is best demonstrated by having the esophageal hiatus dependent to the stomach and by applying pressure to the stomach during roentgenography. The use of a hard, rather narrow and rounded cushion, upon which the patient lies prone, is of considerable aid in obtaining an improved examination. This cushion, which we call the tootsie-roll, automatically places the patient in a semi-Trendelenburg position; his weight resting on the cushion adds pressure to the anterior abdominal wall and indirectly to the stomach. By employing such a procedure during the past several years, we were able to demonstrate more esophageal hiatus hernias of the stomach than previously and the esophagus was more easily visualized since the barium remained in its lower third for a longer period.

The method was apparently first described by Wolf and Guglielmo.[6] Later Heilbrun[5] noted that many sliding hernias, as well as other small protrusions (probably also hernias) which were not otherwise demonstrated, became visible with this procedure and that previously demonstrated hernias were accentuated by the maneuver. Our observations are similar.

METHOD

The placement of the hard cushion is important. The patient should rest on it in a slightly oblique position, left side down, with the cushion midway between the costal margin and the wing of the ilium (Fig. 1 and 2). Not every patient can tolerate the device; it is not used where there is active bleeding, or in the patient who is elderly and feeble.

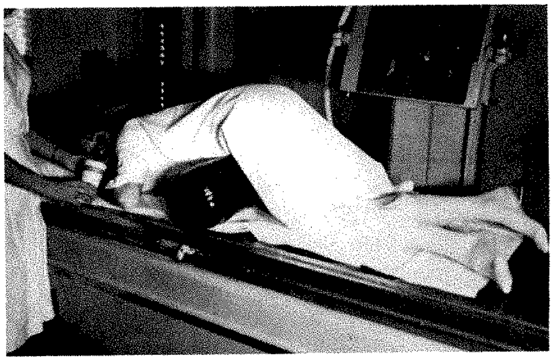


Fig. 1. Photograph showing the patient in the oblique position with the hard cushion placed between the ilium and costal margin.

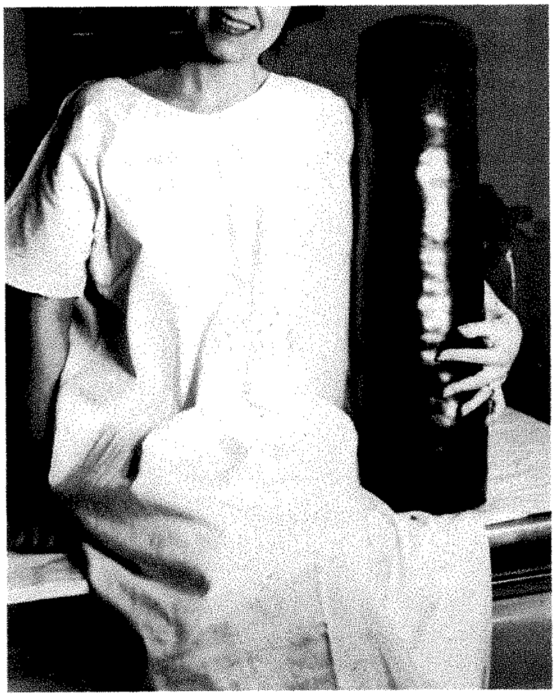


Fig. 2. The size and shape of the hard cushion are shown. Shorter ones are sometimes more convenient, depending on the size of the patient.

In order to obtain an accurate evaluation of the method, 100 consecutive upper gastrointestinal tract examinations were carried out in such a manner as to allow a comparison of spot roentgenograms of the lower

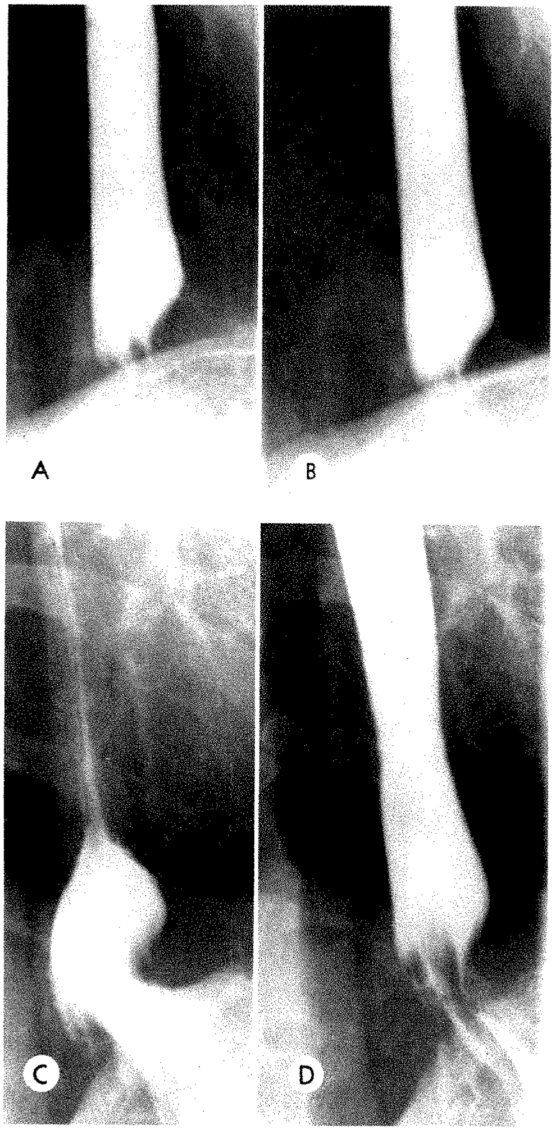


Fig. 3. Thirty-one year old white man with an "ulcer" history. (*A* and *B*) Spot roentgenograms were interpreted as normal. (*C* and *D*) Roentgenograms with the cushion in place possibly show a hernia but were considered questionable.

esophagus with and without the cushion in place. The patients were all ambulatory referrals in an office radiologic practice. During the fluoroscopic examination, they were placed in the prone position, asked to swallow liquid barium and, with the barium in the lower esophagus, to take a deep breath and hold it. Two spot roentgenograms were made on one film. The same procedure was repeated after the patient was placed on the cushion. The 400 spot roentgenograms were then studied in pairs independently and jointly by three of us.*

Without using any clinical information, the roentgenograms were classified into 1 of the following 6 categories: (1) No hernia on any roentgenograms; (2) no hernia on routine roentgenograms, questionable hernia on cushion technique roentgenograms; (3) no hernia on routine roentgenograms, definite hernia on cushion technique roentgenograms; (4) questionable hernia on routine

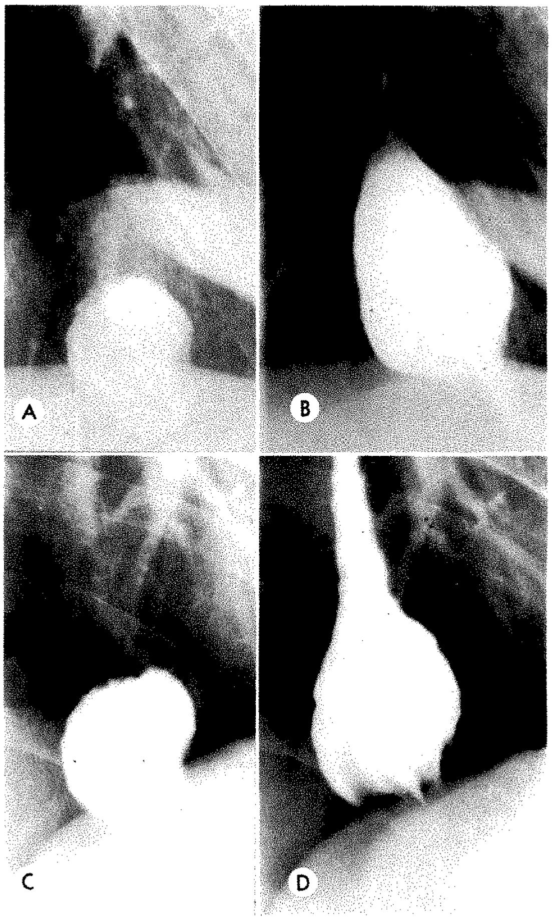


Fig. 4. Thirty-six year old white man with vague upper gastrointestinal tract complaints. (*A* and *B*) Spot roentgenograms were considered normal. (*C* and *D*) Roentgenograms with the cushion in place were considered questionable or suggestive of the presence of hiatus hernia.

---

* William F. Weller, M.D., and Reuben D. Knopf, M.D. assisted with the interpretations.

roentgenograms, definite hernia on cushion technique roentgenograms; (5) hernia on all roentgenograms, cushion technique roentgenograms demonstrating it better than the others; and (6) hernia on all roentgenograms, no difference in demonstration.

RESULTS

In the group of 100 patients, it was found that in 63 no hernia was visualized on

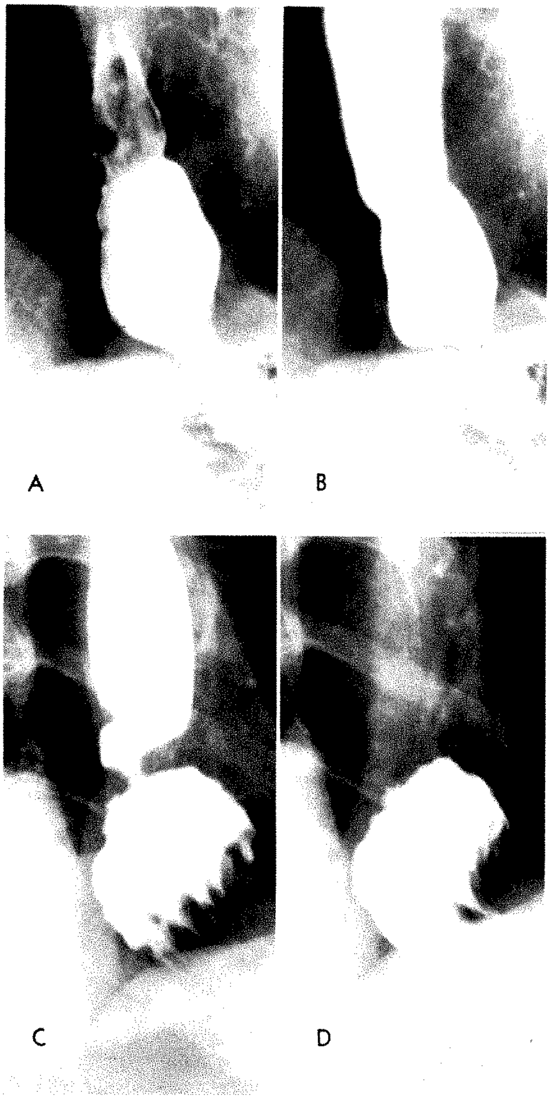


Fig. 5. Sixty-seven year old white woman. (*A* and *B*) Spot roentgenograms were believed to be normal. (*C* and *D*) With the cushion technique there is conclusive evidence of hiatus hernia.

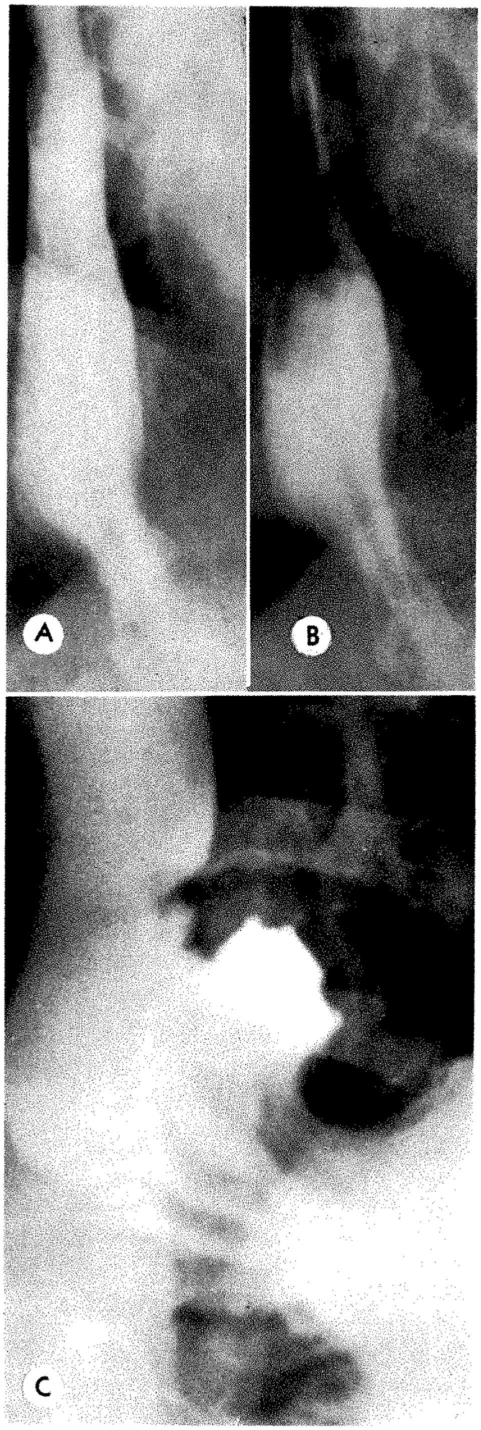


Fig. 6. Twenty-four year old white woman who had nausea and upper abdominal pain. (*A* and *B*) Spot roentgenograms were believed to be normal. (*C*) Roentgenogram with the cushion in place shows conclusive evidence of hiatus hernia of the stomach.

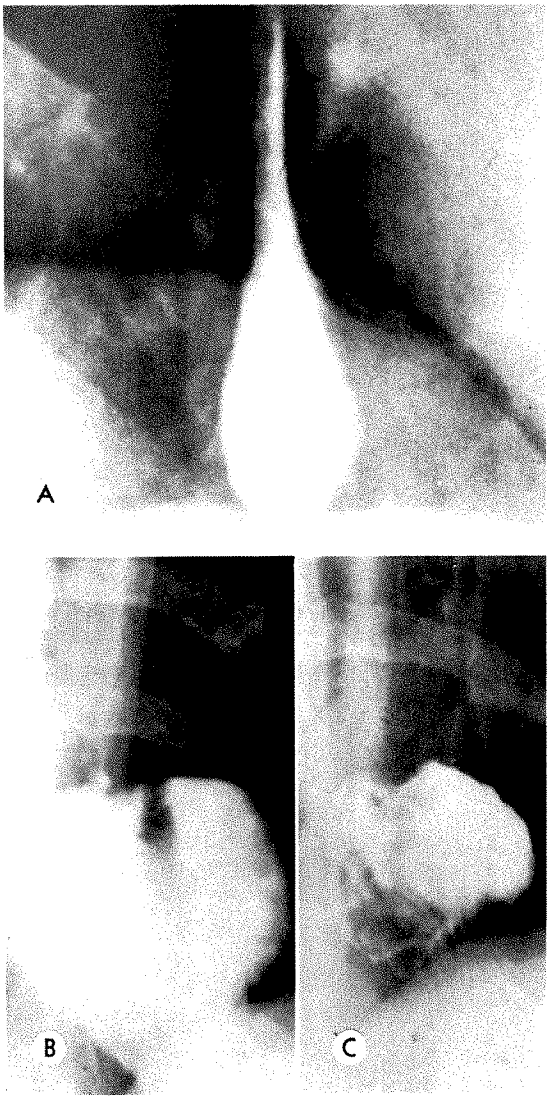


Fig. 7. Fifty-three year old white woman with symptoms of vomiting and severe substernal pain. (*A*) Spot roentgenogram was believed to be normal. (*B* and *C*) Roentgenograms with the cushion technique demonstrate esophageal hiatus hernia of the stomach.

roentgenograms either with the use of pressure or without it. Nine demonstrated a questionable hernia when pressure was applied (Fig. 3, *C* and *D;* and 4, *C* and *D*). Seventeen showed a definite hernia on roentgenograms when the cushion was used but not on the others (Fig. 5, *C* and *D;* 6 *C;* and 7, *B* and *C*).

Two patients demonstrated a questionable hernia on roentgenograms without the use of a cushion and a definite one when pressure was used.

There were 7 patients showing a definite hernia on all roentgenograms, but it was

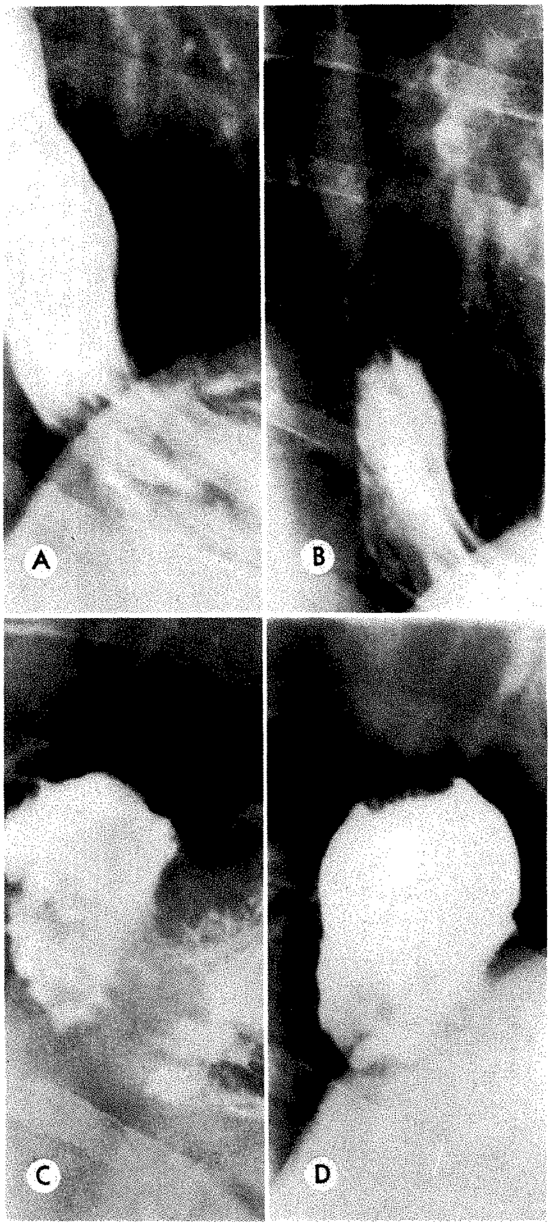


Fig. 8. Forty-seven year old white male thoracic surgeon who suspected the presence of a hiatus hernia. (*A* and *B*) Spot roentgenograms were believed to show a hernia. (*C* and *D*) Roentgenograms made with the cushion in place conclusively demonstrate its presence.

much better demonstrated when pressure was applied (Fig. 8, *A–D;* 9, *A–D;* and 10, *A–D*). In 2 patients a hernia was visualized on all roentgenograms with no difference in the demonstration.

A tabulation of the results is given in Table I. Table II shows the age distribution of the patients, which ranged from 19 to 79 years.

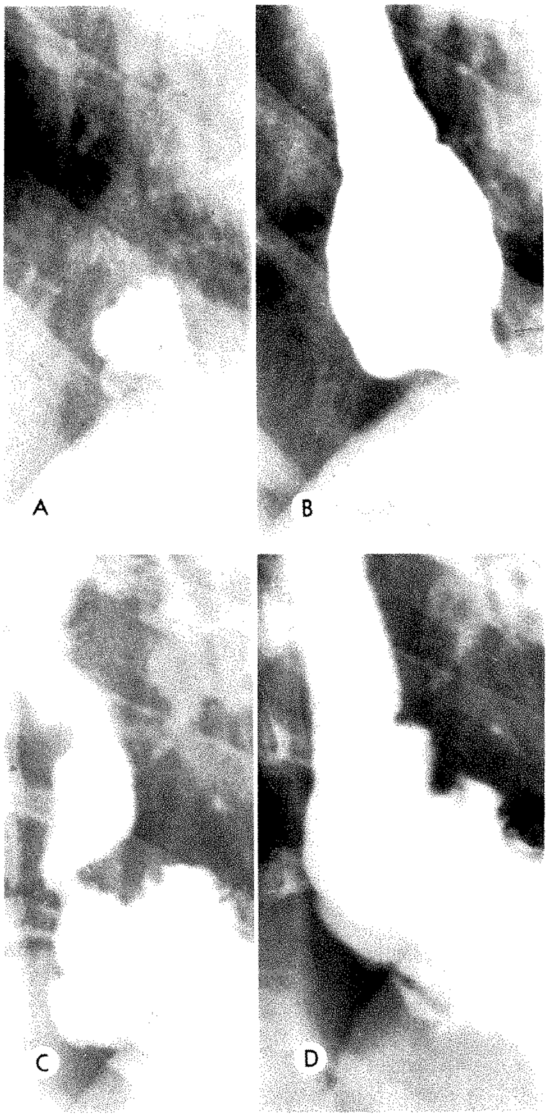


Fig. 9. Forty-one year old white woman. (*A* and *B*) Roentgenograms were believed to show a hiatus hernia. (*C* and *D*) There was considerable improvement in the demonstration of a hernia when the cushion technique was used.

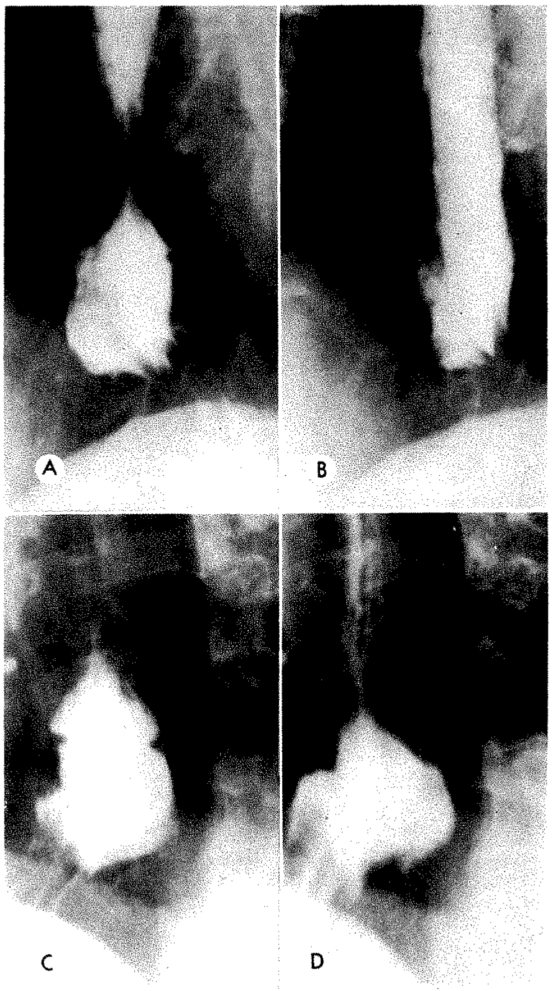


Fig. 10. Thirty-seven year old white man who had substernal pain and burning. (*A* and *B*) Roentgenograms were believed to show a hiatus hernia. (*C* and *D*) There was improvement in the demonstration of the hernia when the cushion technique was used.

DISCUSSION

From these observations we believe that in 17 out of a group of 100 patients, a diagnosis of esophageal hiatus hernia was made because of the use of the cushion; we believe that in another 9 cases the use of the cushion aided in the diagnosis of hernia. If the patients with a questionable hernia are included with those in whom a definite hernia was demonstrated, then in our series of 100 consecutive patients, 26 per cent had a demonstrable hernia when the cushion

TABLE I

Category	No. of Cases
1. No hernia on any roentgenograms	63
2. Cushion technique roentgenograms questionable	9
3. No hernia on routine roentgenograms Hernia on cushion technique roentgenograms	17
4. Questionable hernia on routine roentgenograms Hernia on cushion technique roentgenograms	2
5. Hernia on all roentgenograms Better demonstration on cushion technique roentgenograms	7
6. Hernia on all roentgenograms No difference on any roentgenograms	2
	100

TABLE II

Age*	No Evidence of Hiatus Hernia	Evidence of Hiatus Hernia
9–19	/	/
20–29	///////	////
30–39	/////////////////////	////
40–49	///////////	////////
50–59	////////////	///////
60–69	/////////	///
70–79	//	/

* 9 questionable cases not included.

technique was used. Braucher, Van Woert and Kirsner,[2] in referring to the work of Hafter[4] and Brick,[3] stated that the reported incidence of hiatus hernia in different groups of patients ranges from 0.5 to 12.5 per cent; however, these figures are not entirely representative since they are limited to patients with digestive symptoms and do not include the study of all patients. Andersen and Effler[1] reported that in a group of patients who were subjected to roentgenologic evaluation, 8 to 10 per cent had hernias, with the greatest frequency in overweight patients between 40 and 70 years of age. It appears that the incidence among our patients, using the pressure device, is much higher than this. We made no attempt to correlate clinical information with these results.

CONCLUSION

By the use of a hard, round cushion to obtain increased abdominal pressure, in 19 out of 100 patients a hiatus hernia, which would not have been discovered by ordinary fluoroscopy and spot roentgenography of the esophagus, was visualized. There was improved demonstration of the hernia in another 9 patients.

2037 Crystal Spring Avenue
Roanoke, Virginia

REFERENCES

1. Andersen, H. A., and Effler, D. B. Esophageal hiatus hernia. *Postgrad. Med.*, 1958, *23*, 331–336.
2. Braucher, R. E., van Woert, M., and Kirsner, J. B. Esophageal hiatus hernia. *Postgrad. Med.*, 1962, *31*, 325–331.
3. Brick, I. B. Incidence of hiatus hernia and associated lesions diagnosed by roentgen ray. *Arch. Surg.*, 1949, *58*, 419–427.
4. Hafter, E. Hiatal hernia; its diagnosis and clinical significance. *Am. J. Digest. Dis.*, 1958, *3*, 901–915.
5. Heilbrun, N. Radiologic study of cardioesophageal area. *New York J. Med.*, 1958, *58*, 3280–3283.
6. Wolf, B. S., and Guglielmo, J. Method for roentgen demonstration of minimal hiatal herniation. *J. Mt. Sinai Hosp.*, 1956, *23*, 738–741.

* * *

THE LOWER ESOPHAGEAL RING*

LONG TERM FOLLOW-UP OF SYMPTOMATIC AND ASYMPTOMATIC RINGS

By RICHARD SCHATZKI, M.D.
CAMBRIDGE, MASSACHUSETTS

IN HIS description of the lower esophagus, Templeton,[14] in 1944 mentioned an *asymptomatic* diaphragmatic narrowing in the lower esophagus. In 1947 the present author saw a patient who had had repeated episodes of dysphagia. A ring like narrowing in the lower esophagus—similar to that described by Templeton—was the only demonstrable abnormality and appeared to be the cause for the patient's symptoms. Since then, the entity of the *symptomatic* lower esophageal ring has become securely established. The first reports of symptomatic cases were published in 1953 by Ingelfinger and Kramer[4] and by Schatzki and Gary.[9]

The roentgen appearance and behavior of the esophageal ring have been well studied.[6,8,10] It is not an abnormal contraction but rather an area of restricted distensibility.[10] It lies at the junction of the esophageal and gastric mucosa.[5,7,11,16,17] To the best of our knowledge, it represents the junction of esophagus and stomach. This opinion, although shared by most observers,[1,2,6,8,12,13,16] is not agreed upon by all.[3]

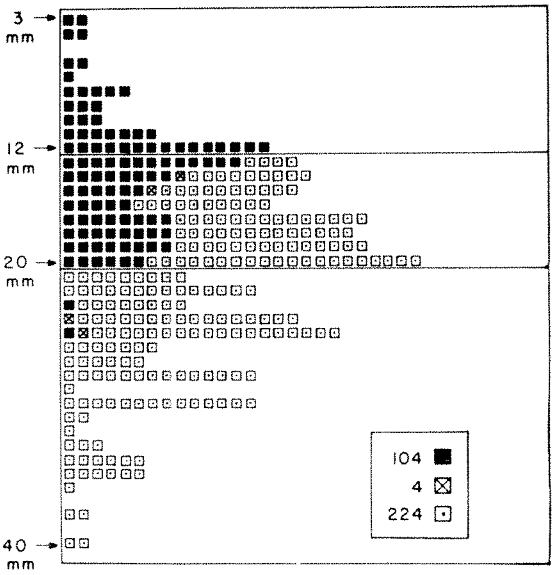


Fig. 1. Chart showing the relationship between dysphagia and diameter of the rings of the various patients. It refers to the maximal diameter of the rings at the time of their first demonstration, as measured on the spot roentgenograms. The black squares represent the 104 patients with repeated episodes of dysphagia, the squares with diagonals the 4 patients with only one episode of dysphagia, and the dotted squares 224 patients without dysphagia. (By no means were all asymptomatic patients with rings catalogued, and for this reason many are not seen on this chart).

In some patients, the esophageal ring causes characteristic episodes of dysphagia; in others it does not. Figure 1 gives a graphic tabulation of 104 cases of esophageal rings with episodic dysphagia which were seen before July, 1962 by the author and also includes some but not all asymptomatic cases seen in the same period of time. It shows that the maximum diameter of the individual esophageal ring is the most decisive factor in determining whether or not it causes dysphagia. We have never seen an esophageal ring with an original diameter of less than 13 mm. which did not cause symptoms, and there were only 2 patients in whom a ring larger than 20 mm. caused repeated episodes of dysphagia. Eating manners play an additional though less important role.

Even though the majority of individuals with esophageal rings have no dysphagia, the lower esophageal ring is, in our experience, the most common cause of episodic dysphagia.

Very little is known about the later

---

* From the Department of Radiology, Mount Auburn Hospital, Cambridge, Massachusetts.
Read in part as the George W. Holmes Lecture of the New England Roentgen Ray Society, Boston, May, 1962, and at the Tenth International Congress of Radiology, Montreal, Quebec, Canada, August 26–September 1, 1962.

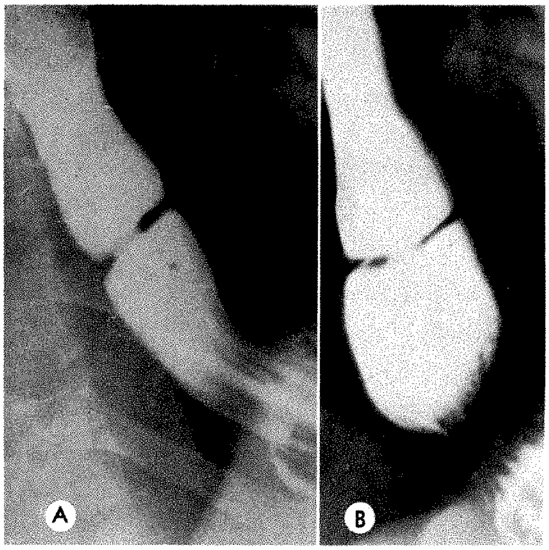


FIG. 2. Ten years' observation of an 8 mm. symptomatic ring. The ring has remained unchanged in diameter as did the episodic dysphagia. (*A*) 1952. (*B*) 1962.

course of esophageal rings in symptomatic and asymptomatic patients. Our initial impression was that once the esophageal ring occurred it changed very little in size and shape, and that the symptoms remained fairly constant. Recently, follow-up studies were made to examine the validity of this initial impression, and to ascertain whether a symptomatic esophageal ring is the same basically as the asymptomatic esophageal ring or whether the two are different lesions. We were also interested in finding whether, as in some cases with hiatus hernias, areas of disturbed distensibility exceeding the length of the initial ring did develop, indicating subsequent esophagitis with mural fibrosis.

Sixty-six patients were re-examined who had initially demonstrated esophageal rings more than 5 years previous to this study. In almost half of these patients (31), the actual follow-up extended over a period of more than 7 years. Thirty of the 66 patients had had episodic dysphagia when first seen, while 36 had been asymptomatic. Figures 2 through 7, inclusive are roentgenograms of some of these patients.

No appreciable change was noted in 19 of the 30 patients who were symptomatic when originally examined while in 11, the esophageal ring showed a decrease in size.* In only 4 patients was there an aggravation of symptoms; in 12 patients they remained essentially unchanged and in 14, or almost one-half of the patients, the symptoms had actually improved (Tables I and II).

Several factors contributed to this im-

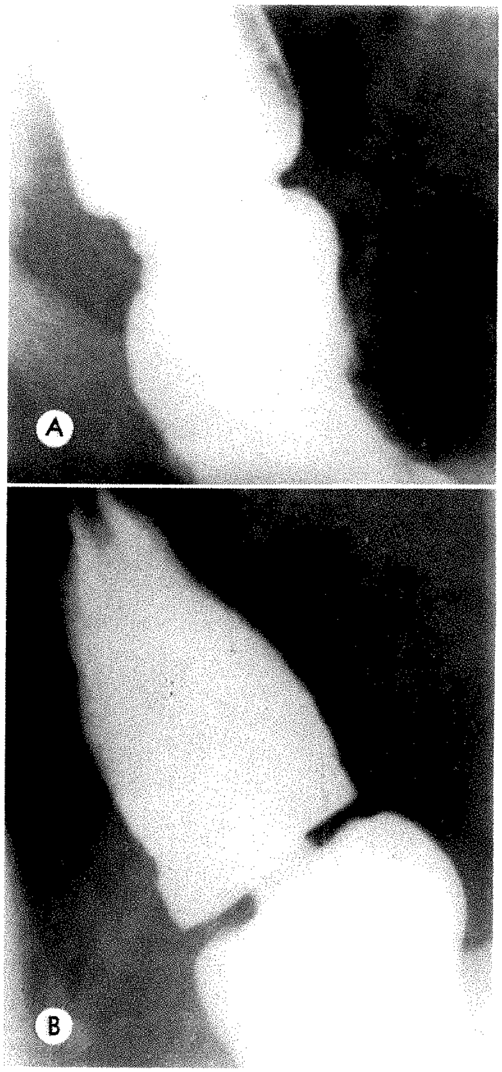


FIG. 3. Considerable decrease in the size of a symptomatic ring during 9 years without increase in frequency and severity of symptoms. (*A*) 1953: 20 mm. (*B*) 1962: 12 mm.

---

* Only a decrease or increase in ring size of more than 20 per cent was called a change. The diameter of the ring was measured on spot roentgenograms.

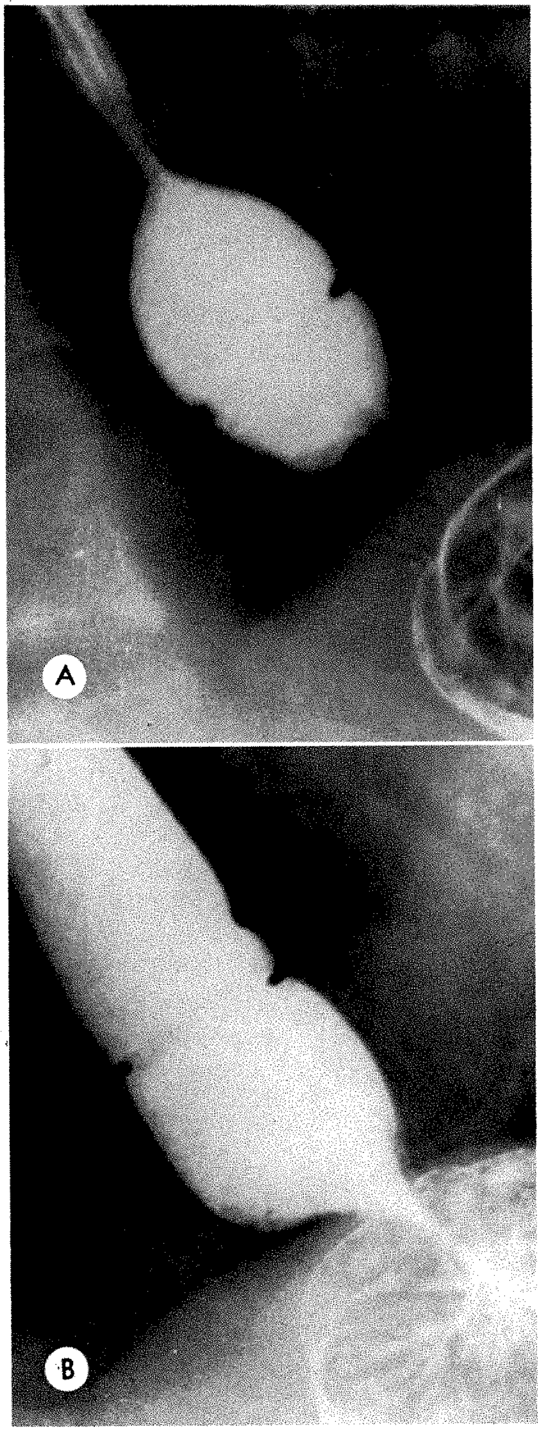


FIG. 4. Asymptomatic ring unchanged in size in 8 years. The patient never had any episodes of dysphagia. (*A*) 1954: 25 mm. (*B*) 1962: 24 mm.

TABLE I

DIAMETERS OF 30 SYMPTOMATIC RINGS

5 OR MORE YEARS LATER	
Unchanged	19
Decreased	11

TABLE II

SYMPTOMS IN 30 SYMPTOMATIC RINGS

5 OR MORE YEARS LATER	
Unchanged	12
Decreased	14
Increased	4

provement which in a number of cases occurred in spite of the fact that the esophageal ring had actually decreased in diameter. Most of the patients ate more carefully after they knew the cause of their symptoms, and in addition, some of the patients, originally quite frightened by the episodes of sudden dysphagia, paid less attention to them after they had been informed about the rather benign reason for this difficulty.

The diameters of the esophageal rings in the 36 asymptomatic cases had originally varied from 13 mm. to 32 mm. When reexamined more than 5 years later, the size of the esophageal ring had remained essentially unchanged in the majority of the cases (27). In 8, the diameter had decreased by more than 20 per cent and in 1 the diameter of the esophageal ring had increased so much that it was questionable whether an

TABLE III

DIAMETERS OF 36 ASYMPTOMATIC RINGS

5 OR MORE YEARS LATER	
Unchanged	27
Decreased	8
Increased	1

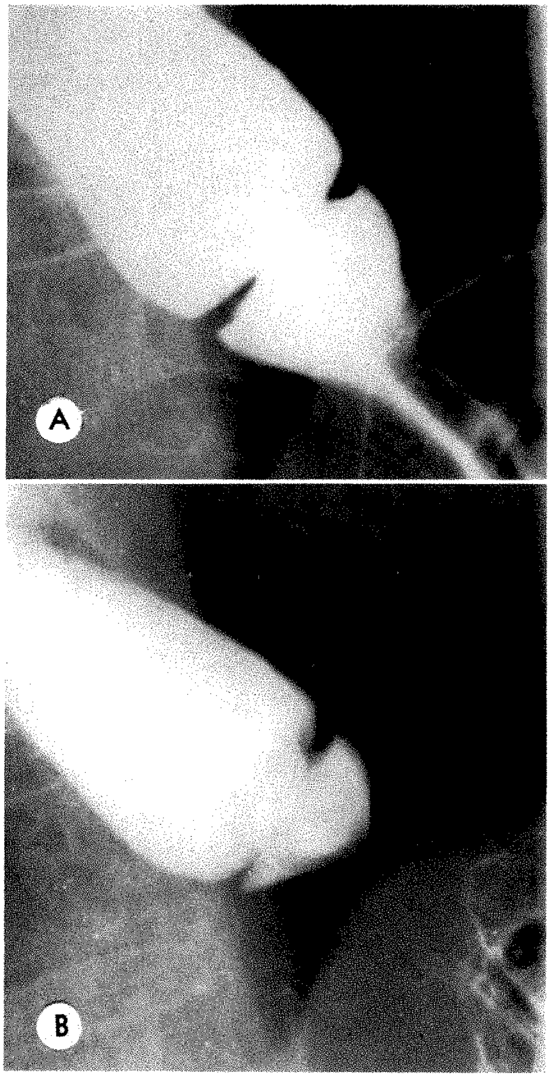


FIG. 5. Narrow (13 mm.) asymptomatic ring which did not change in diameter over a period of 7 years. (*A*) There was no dysphagia in 1955 and (*B*) none in 1962. Patient was a slow eater. This is the narrowest ring without symptoms which we have seen.

esophageal ring still remained (Fig. 7, *A*, *B*, and *C*). This was the only case in which the presence of the esophageal ring was doubtful at the later examination (Table III).

Broadly, the changes in the size of the esophageal rings of the asymptomatic cases were rather similar to those in the symptomatic ones. In about one-fourth of the asymptomatic cases, the diameter had decreased as compared to one-third in the symptomatic group. Significant, however, was the fact that, although 32 of the 36 initially asymptomatic patients were still asymptomatic, characteristic episodic dysphagia had developed in 4 of the group in

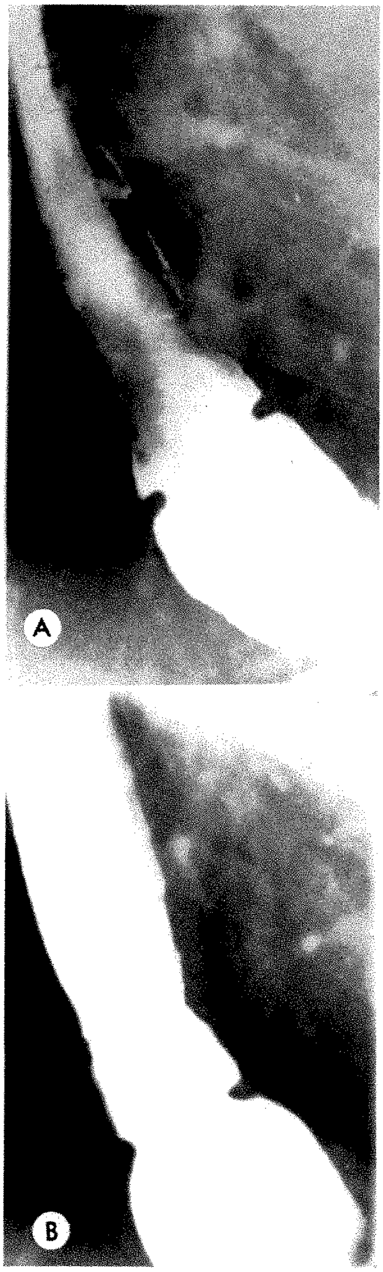


FIG. 6. Asymptomatic ring which later developed symptoms. (*A*) 1950: 20 mm. ring. No symptoms. (*B*) 1962: ring measures 18 mm. Two-year history of occasional dysphagia.

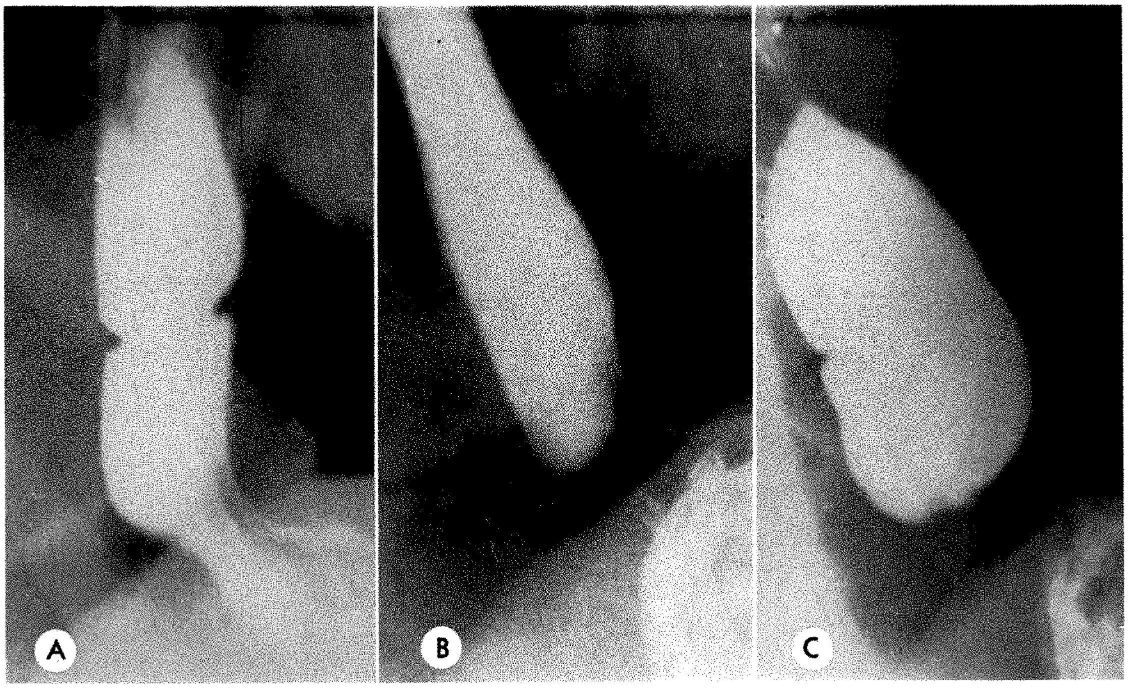


FIG. 7. (*A*) 1952: asymptomatic ring which either had disappeared or had markedly increased in diameter 10 years later. (*B*) 1962: no ring visible although the esophagus is slightly more distended than in 1952. (*C*) With greater distention a questionable ring is seen. This is the *only* ring which, in our experience, either considerably increased in width or possibly was absent at a later examination.

the intervening years (Table IV). In 2 of these, there was, according to our classification (see footnote on page 806), no change in the ring size (from 20 mm. to 18 mm. in 1 case, and from 18 mm. to 15 mm. in the other), while there was a decrease in ring size in the other 2 (from 14 mm. to 6 mm. in 1, and from 19 mm. to 15 mm. in the other). If a change of less than 20 per cent had been considered, there would be some decrease in the size of the esophageal rings in all 4 cases. It thus appears that patients with asymptomatic esophageal rings may develop symptoms when the ring becomes too narrow for that particular patient, or occasionally perhaps when the patient changes his eating habits.

As regards the possible secondary development of esophagitis with fibrosis of the wall, the follow-up studies showed that no elongated areas of rigidity, as seen in patients with reflux esophagitis, developed in these patients.

CONCLUSION

1. The lower esophageal ring is the most reliable landmark of the esophagogastric junction.
2. The esophageal ring is the most common cause of repeated episodes of dysphagia.
3. A long term follow-up on 66 patients who demonstrated esophageal rings has revealed that there is a tendency for both, the symptomatic and asymptomatic, rings to decrease in diameter although the majority of the esophageal rings remain unchanged in size.
4. Asymptomatic patients with esophag-

TABLE IV

STATUS OF 36 ASYMPTOMATIC RINGS

5 OR MORE YEARS LATER	
Still asymptomatic	32
Developed symptoms	4

eal rings may develop dysphagia. In other words, there is no basic difference between the lower esophageal rings in patients with or without dysphagia.

1180 Beacon Street
Brookline 46, Massachusetts

REFERENCES

1. Bartlett, M. K., and Jones, C. M. Surgical experience with lower esophageal ring. *Ann. Surg.*, 1959, *149*, 491–497.
2. Gould, D. M., and Barnhard, H. J. Changing concepts in structure, function and disease of lower esophagus. *Am. J. M. Sc.*, 1957, *233*, 581–595.
3. Harris, L. D., Kelly, J. E., Jr., and Kramer, P. Relation of lower esophageal ring to esophagogastric junction. *New England J. Med.*, 1960, *263*, 1232–1235.
4. Ingelfinger, F. J., and Kramer, P. Dysphagia produced by contractile ring in lower esophagus. *Gastroenterology*, 1953, *23*, 419–430.
5. Keyting, W. S., Baker, G. M., McCarver, R. R., and Daywitt, A. L. Lower esophagus. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1960, *84*, 1070–1075.
6. Kleinfelder, H., and Longin, F. Der untere Oesophagusring. *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, 1961, *95*, 610–623.
7. MacMahon, H. E., Schatzki, R., and Gary, J. E. Pathology of lower esophageal ring: report of a case with autopsy, observed for nine years. *New England J. Med.*, 1958, *259*, 1–8.
8. Potsaid, M. S., Irie, G., and Griscom, N. T. Motility changes revealing esophagogastric junction. *Radiology*, 1961, *76*, 262–263.
9. Schatzki, R., and Gary, J. E. Dysphagia due to diaphragm-like localized narrowing in lower esophagus. ("Lower esophageal ring.") Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1953, *70*, 911–922.
10. Schatzki, R., and Gary, J. E. Lower esophageal ring. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1956, *75*, 246–261.
11. Schatzki, R., and Gary, J. E. Unpublished data.
12. Som, M. L., Wolf, B. S., and Marshak, R. H. Narrow esophagogastric ring treated endoscopically. *Gastroenterology*, 1960, *39*, 634–638.
13. Stauffer, H. M., Bonakdar-Pour, A., and Woloshin, H. J. Brief massive spasm of distal esophagus greatly increasing gastric herniation, documented cineradiographically in patient with lower esophageal ring. *Gastroenterology*, 1960, *38*, 637–640.
14. Templeton, F. E. X-Ray Examination of the Stomach: A Description of the Roentgenologic Anatomy, Physiology and Pathology of the Esophagus, Stomach and Duodenum. University of Chicago Press, Chicago, 1944, pp. 106, 112.
15. Van Fleit, W. E., and Abbott, O. A. Management of esophageal hiatal hernia complicated by lower esophageal ring. *Am. Surgeon*, 1959, *25*, 670–673.
16. Wilkins, E. W., Jr., and Bartlett, M. K. Surgical treatment of lower esophageal ring. *New England J. Med.*, 1963, *268*, 461–464.
17. Wolf, B. S. Case No. 114. *J. Mt. Sinai Hosp.*, 1960, *27*, 545–547.

THE ANATOMIC BASIS FOR THE LOWER ESOPHAGEAL CONTRACTION RING*

PLICATION THEORY AND ITS APPLICATIONS

By O. ARTHUR STIENNON, M.D.
MADISON, WISCONSIN

THE lower esophageal "contraction ring" is a fairly common condition with a variety of unusual features, virtually none of which has as yet been explained. At the same time, the clinical symptoms, the roentgenologic appearance and the clinical course have been well described in the literature[2,4,5,9,10] and there is sufficient anatomic information already at hand that no new laboratory or clinical data are required to formulate a mechanism, or, having formulated one, to test it.

Any mechanism proposed must give a reasonable account of certain salient features of the disease and can also be tested by requiring that it explain a number of the clinical, roentgenologic anatomic observations which have been recorded.

1. It is evident that the mechanism must be in agreement with the anatomic substrate. For example, one cannot postulate a sphincter muscle if in actuality no such sphincter exists.

2. The high association of contraction rings with esophageal hiatus hernias must be accounted for. It would not be going too far to say that the contraction ring is invariably associated with a hiatus hernia. This association has impressed every writer on the subject and, although the literature does not reflect a perfect correlation between the two conditions, I believe this is due to somewhat overly stringent criteria for diagnosing hiatus hernias, to the deficiencies of the current explanations for contraction rings and to an erroneous "two-pouch theory" of the lower esophagus. As a matter of fact, from a practical point of view it has become almost axiomatic to many radiologists that if a contraction ring is demonstrated a hiatus hernia is present by definition.

3. An accurate theory must take into account the fact that evidence of inflammatory disease is singularly lacking in anatomic specimens and on endoscopy. The same applies to the fact that, much as this resembles a fibrous tissue contraction, pathologically such fibrous tissue collections have not been demonstrated.

4. With the proper technique, these rings are rather easily demonstrated by the radiologist and one would be led to think from their quite constant appearance that there would be no problem in demonstrating them with the esophagoscope. The fact is, however, that most of the time the esophagoscopist sees nothing abnormal during his examination.

If the proposed mechanism accounts for these four leading features of the condition, it is then possible to test it further by seeing how well it answers the following questions:

1. *Why is the ring seen only with distention of the esophagus?* Almost invariably, the ring simply vanishes when the esophagus contracts to its normal caliber after being distended during the course of the fluoroscopic examination.

2. *How can one explain the overnight onset of symptoms?*

3. *Why is there no progression?* Repeated observations which now cover intervals of 9 years[7] or more have failed to show any significant increase in the narrowing of the esophageal lumen.

4. *Why does dilatation fail to afford any significant relief in the greater portion of the patients?*

5. *Why does the ring occur precisely at the cardioesophageal junction?*

---

* From the Department of Radiology, St. Mary's Hospital, Madison, Wisconsin.

To these criteria we could add as a supreme test to be met by any new theory that it provide a true rationale for treatment.

A number of explanations have been put forward for the genesis of contraction rings. Of these, the easiest to deal with is the postulation of a fibrous connective tissue ring. This mechanism fails primarily because it is in conflict with the histologic findings. Secondarily, it fails to explain any of the other features of the disease. For example, such a ring should be quite constant and there should be no difficulty in demonstrating it esophagoscopically, it should not produce intermittent symptoms, and so on.

Against inflammatory disease as the underlying cause is the failure to find histologically any evidence of an inflammatory reaction. The chief appeal of this mechanism is that if there were such inflammation, it would be relatively easy to explain as due to the hiatus hernia which invariably accompanies the ring; that is, the hiatus hernia produces cardioesophageal reflux which in turn produces inflammation and the latter results in the ring. Here one has to gloss over the question of why a hiatus hernia *per se* should cause cardioesophageal reflux, the answer to which is not at all obvious. After all, if there is a sphincter mechanism for the lower esophagus, why should it depend on being in or below the hiatus for efficient operation? Perhaps we should require a new theory to account for this as well. Even if we could explain away all of these deficiencies of the inflammatory theory, there is the final indisputable fact that inflammation of the esophagus is esophagitis, a disease in its own right which has no resemblance whatsoever to a cardioesophageal ring. Logically, the same mechanism cannot be used for two different diseases in the same location.

The theory which has received most serious attention is the suggested presence of an inferior constrictor of the esophagus. Although it is difficult to evaluate the morphologic evidence for and against such a sphincter,[6] and the issue can easily become fogged by the question of how many muscle cells are required to form a physiologically effective sphincter, it can be shown on logical grounds that any possible sphincter muscle in this region could not give a true account of the ring. There are only three muscle layers: the muscularis propria with its inner circular and outer longitudinal layers, and the muscularis mucosae. The longitudinal layer of the muscularis propria cannot have a constricting action because of the direction of its fibers, nor can the muscularis mucosae, the fibers of which are *exclusively longitudinal.*[11] There remain, therefore, only the circular fibers of the muscularis propria, and these are already spoken for by another disease—esophageal "achalasia." One can attempt to get around these realities by putting forward the "bracket" bundles and theorizing that if only these contracted an appearance different from achalasia would result. It is hard to believe that the innervation is this selective, but even if one could, there is the further difficulty that these are described as being spirally arranged[15] and therefore would have to produce a helical, not a transverse, ring.

These difficulties have prompted a very thorough investigation into the minutia of the phrenoesophageal membrane,[15] but this structure can only pull, not push, and that only under special circumstances. Hence it cannot produce a constriction of the esophageal lumen. Finally, the postulation of sphincters falls into the category of *ad hoc* theory. At best it can only explain a single feature of the disease—the constriction of the lumen—and to account for the other salient features more and more assumptions have to be made which fail under empirical and logical tests.

Doubtless, considerations of this type have led more than one student of the disease to conclude that the origin of the ring is unknown.

A NEW THEORY

Let us assume that for some reason the esophagus shortens by an appreciable amount, say 1 to 3 inches. What *a priori* predictions can we make about its various elements? It is self evident that all layers have to contract equally or one of them will be redundant. The only layer of the organ which is not naturally constructed to contract is the lamina propria of the mucosa itself. The outer layers are muscle, the muscularis mucosae can be presumed to contract, and there are elastic connective tissues even in the submucosa. If any layer is prone to become redundant, it will certainly be the epithelial layer proper. This extra length accumulates at the distal end of the esophagus as it is pushed ahead of the food bolus, and there forms a plication or a circumferential "accordion pleat." *This is the contraction ring.*

Simple as it seems, this proposed mechanism meets all of the tests we have set up for it. There is now no difficulty in explaining the association with hiatus hernia. Indeed, the hiatus hernia explains the ring. Herniation has to occur before the esophagus can shorten, and is a prediction of the plication theory. There is no longer any need to search for a sphincter muscle, as the plication already accounts for the narrowed lumen and much more accurately. After all, a sphincter should produce an "hourglass" narrowing, not the perfectly straight, thin, transverse narrowing of the lumen which one actually sees at the fluoroscope. Moreover, plication accounts for the hitherto unexplained fact that in the autopsied case of McMahon *et al.*[7] there was only lamina propria in the web. These authors further report that the muscularis mucosae was split into three layers in the region of the ring. None of these layers are sufficiently well developed to constrict the esophagus. Our theory predicts that the mucosa will pile up in a redundant fold, and when this occurs something has to yield. Since the longitudinal cells of the muscularis mucosae provide the best plane of cleavage, it is natural that the splitting should occur in this layer.

Among our simple assumptions there was no need to include inflammation, so the lack of inflammatory changes in surgical and postmortem specimens is not surprising, nor is it at all remarkable that the esophagoscopist cannot identify a web. These patients are generally examined under anesthesia, which certainly produces a relaxation of the contracted esophagus and the organ is sufficiently stretched by instrumentation to iron out any residual redundancy of the mucous membrane.

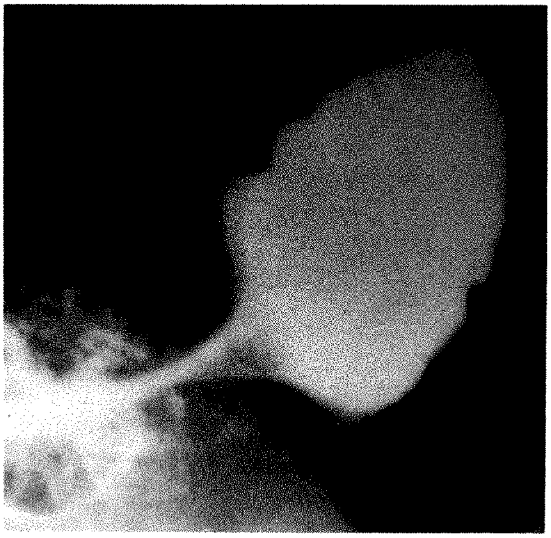


Fig. 1. Because we strive to demonstrate them that way, the rings are single and deep. Shown here are two shallow rings, both due to plications of redundant lamina propria of the esophageal mucosa.

Despite its success in explaining the above features, the new theory seems to fail when applied to one very important fluoroscopic observation. All observers agree that these rings are best seen when the lower esophagus is well distended. One would think that if the mucosa were redundant, ballooning of the lower esophagus would stretch it. Even though the ballooning increases only the transverse diameter, there should be enough increase in the *area* to obliterate a plication only 1 to 10 mm. in height, and yet the plication certainly is not obliterated.

Nevertheless, what at first seems to be a total defeat of the new theory actually turns out to be a signal confirmation. All the more so as it was not even designed to meet this particular observation. The key to the apparent discrepancy is the maneuvers which are actually employed to balloon the lower esophagus.

1. The effect of gravity (which favors emptying) is neutralized or reversed by placing the patient in the horizontal or Trendelenburg position.
2. The Valsalva maneuver is employed to increase intra-abdominal pressure and retard emptying of the esophagus.
3. As an alternative, the Müller maneuver (inspiration with a closed glottis) can be used to decrease intrathoracic pressure and so balloon the esophagus.
4. A large swallow of barium is employed.

It is no coincidence that these are precisely the maneuvers which are used to demonstrate hiatus hernias. In this lies the explanation of the antinomy; these maneuvers demonstrate the ring not because they distend the esophagus but rather in spite of that fact, because by provoking the hiatus hernia they allow the esophagus to shorten and the mucous membrane to plicate. When the hernia reduces, the esophagus lengthens and the ring immediately disappears.

The overnight onset and lack of progression which have proved inexplicable now become quite easy to understand. The ring develops as soon as (1) a sliding esophageal hernia becomes possible and (2) there is sufficient shortening of the esophagus to produce the required degree of redundancy. Both the hiatus hernia and the plication could occur in 24 hours or, if the hiatus hernia developed gradually, the ring would appear when the esophagus was capable of close to maximal shortening. That there is no progression is due to the limited ability to contract of an esophagus which is normal in every way but for its lack of an inferior fixation to the diaphragm.

From what has been said it is evident that we must think of the contraction ring as a dynamic affair, appearing and vanishing from moment to moment as the esophagus contracts or elongates and as the associated hiatus hernia recurs and reduces. This is why the two surfaces of the ring do not appear adherent to each other on microscopic section.

It might well be asked, why does the ring occur at the precise junction of the gastric and esophageal mucosa? For the purposes of ring formation it would seem there is an important anatomic transition distal to this junction. The esophageal mucosa is only loosely attached to the muscular wall, whereas the stomach mucosa is more tightly adherent. Moreover, distal to this point of transition the space between the epithelial layer and the muscularis mucosae instead of being filled with loose connective tissue is densely packed with glandular tubules. If this abrupt transition in character did not occur, it would be more reasonable to predict that prolapse of the redundant epithelial layer would occur, as in general in the gastrointestinal tract prolapse[12] is the preferred mechanism.

The trouble with the sphincter, inflammatory and fibrous tissue theories is that they provide a false rationale for treatment. This ranges from simple dilatation[2] to transthoracic resection of the lower esophagus.[4] Dilatation is bound to be unsuccessful as the bougie, like the esophagoscope, merely obliterates the ring when its passage elongates the esophagus. As soon as it is withdrawn, the ring recurs. Resection of the lower esophagus can hardly fail to be followed by cardioesophageal reflux and in many instances a severe degree of esophagitis, so that the patient's final state may be worse than his first.

We are justified therefore in requiring that the new theory provide a true rationale for treatment. Moreover, we have good reason to believe it does.

If the efficient cause of the ring is shortening of the esophagus, a procedure which restores esophageal length should cure it. The Nissen operation,[8] in which the relatively inelastic lesser curvature is brought down and fixed to the anterior abdominal wall, applies traction to the esophagus through the lesser curvature and corrects the hiatus hernia *and the ring.* The region of the hiatus is not even explored in this quite simple operation. Roentgenologically, it results in a virtually perfect *restitutio ad integrum.*

FURTHER TESTS OF THE PLICATION THEORY

In this way, we have tested the plication theory to the extent possible considering only data obtained from previous observations. There are still other tests which the theory must meet, and I propose to consider first the results of new observations which were suggested by the various implications of the plication mechanism.

It is evident that, although the lower margin of the ring-like plication must be at the junction of the esophageal and gastric mucosa, there is no particular reason for the existence of only one pleat. Thus we would expect that some patients would have several shallow "rings" rather than one deep one. Such auxiliary rings (usually occurring as a small plication proximal to a well-formed deep ring) are a frequent finding in the published cases. In this material it is usually identified as the "inferior constrictor of the esophagus" or the sphincter of Lerche. When demonstrating the ring, one attempts to secure a spot roentgenogram when it is as prominent as possible. If roentgenograms are taken just as the ring begins to form or as it starts to disappear with the emptying of the esophagus, it is a simple matter to record the appearance shown in Figure 1 and 2, *A* and *B*, that of multiple fine plications. The small scallops along the border could hardly be interpreted as anything but multiple "accordion pleats" similar to those formed as one removes a drinking straw from its tubular wrapping.

It also seemed evident that after the Valsalva maneuver was discontinued, having demonstrated the hiatus hernia and ring, if the hernia failed to reduce, as is often the case, the redundant plication of the mucosa should still be present and might be demonstrated by suitably timed exposures. This is somewhat more difficult to do without the advantage of cineroentgenography; however, frequently enough (Fig. 5, *A* and *B;* and 6, *A* and *B*) we have had success in recording a rosette of 4 to 5 mm. polypoid mucosal elevations precisely at the cardioesophageal junction. These, I believe, represent the ring distorted by contraction of the physiologic sphincter of the esophagus. They have been frequently noted in the past but the natural tendency would be to attribute them to a slight buckling or edema of the gastric rugae in the herniated portion of the stomach immediately below. It is evident from the roentgenograms however, that they are quite distinct from these rugae. It is inter-

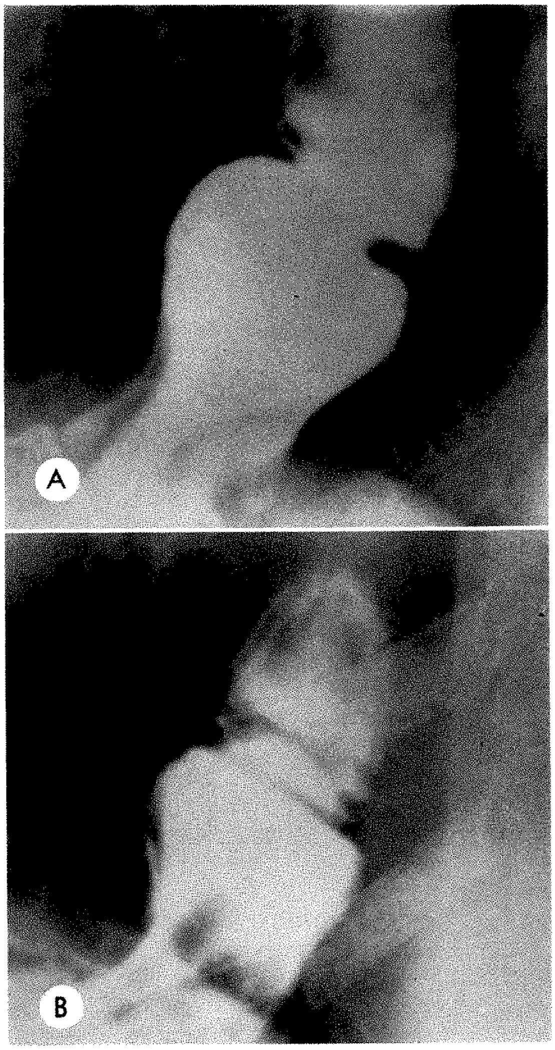


Fig. 2. (*A*) A typical deep ring can break up into several shallow rings. (*B*) Roentgenogram made nearly a year after *A*. Note three fine "accordion pleats" at the cardioesophageal junction.

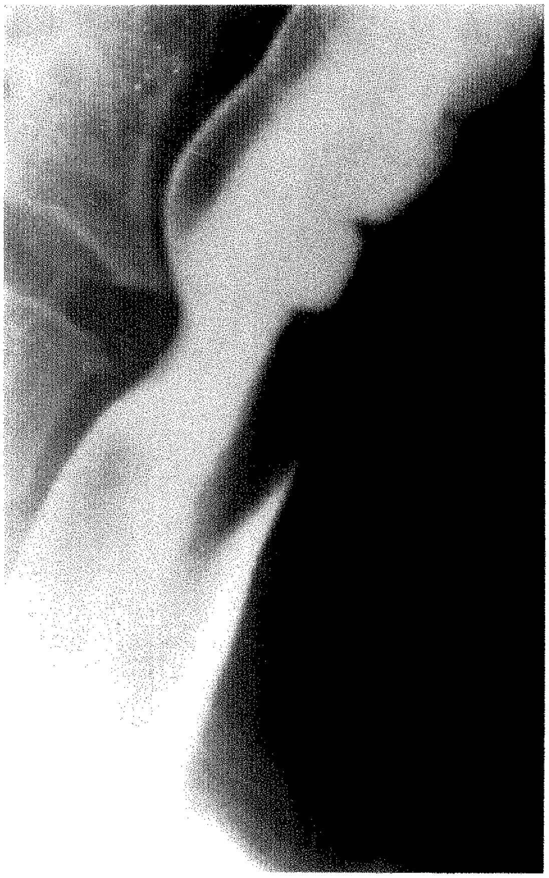


FIG. 3. Upper esophageal webs can also be double. This patient with a hiatus hernia and short esophagus had a double upper esophageal web. She had no iron deficiency anemia or other feature of the Plummer-Vinson syndrome.

esting to note, in view of the "cusp-like" appearance, that the tails of esophageal mucosa extending into the gastric mucosa at this zone of junction may well cause this particular configuration. Even if it were not possible to demonstrate these hemorrhoid-like elevations directly, their presence is practically mandatory from simple mechanical considerations.

A UNIFIED THEORY OF DISEASE OF THE CARDIOESOPHAGEAL JUNCTION

A feature of this new theory of considerable interest is its wider application to other abnormalities situated at the cardioesophageal junction. Schatzki and Gary[10] predicted in their 1956 paper when discussing the problem of the cause of the ring: "The solution of this problem would probably represent a stepping-stone helpful for a better understanding of other problems involving the junction of the stomach and esophagus." This prophesy seems to be amply borne out. Indeed, the clarity and improved understanding which the theory leads to when applied to the other diseases are of more practical significance than the explanation of the contraction ring itself.

THE TWO-POUCH THEORY OF THE LOWER ESOPHAGUS

The first application is on the theoretical level. Figure 7 gives a diagrammatic sur-

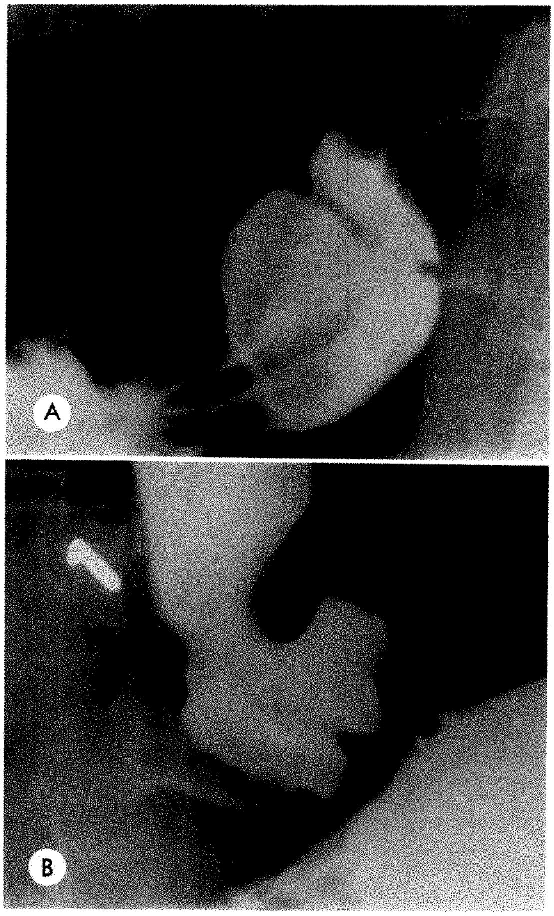


FIG. 4. Despite the hiatus hernia and ring (*A*), the physiologic sphincter of the esophagus is functioning (*B*). When it comes into play, the redundancy is lost as additional length is required to follow the contours of the still dilated phrenic ampulla plus the indentation of the lumen by the sphincter.

vey of the widely, but not universally, accepted two-pouch view of the morphology of the cardioesophageal junction. We are immediately able to reinterpret the diagram as indicated by the alternate set of legends. As the second pouch is undoubtedly the herniated portion of the stomach and as most of the evidence for a subdiaphragmatic esophageal segment is based on the double pouch seen at fluoroscopy, this should dispose of this conception fairly adequately. There are a few other observations which give one the impression of a subdiaphragmatic esophagus but these are faulty. (1) Barium running down two or three gastric rugae when the patient is first examined in the upright position gives the false impression of a subdiaphragmatic continuation of the esophagus. (2) As the esophagus enters the fundus posteriorly and the contour of the fundus follows the diaphragm which is

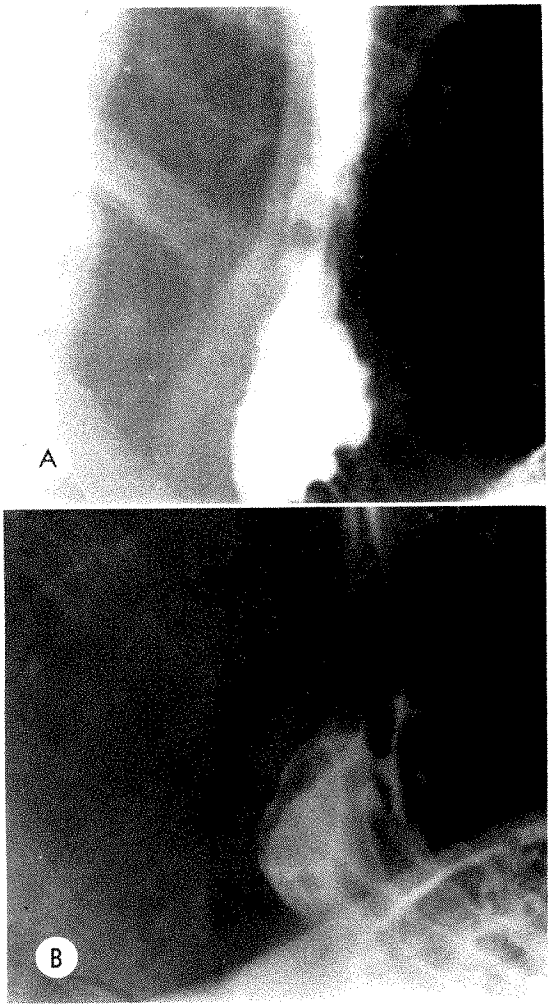


Fig. 5. Mammillary mucosal elevations at the cardioesophageal junction on roentgenograms made after the esophagus has collapsed are consistent with the buckled "ring." It is believed that these obtrude into the lumen when the sphincter contracts and that there is seepage into the lower esophagus from the cardia leading to reflex relaxation of the sphincter and gross reflux. (*A*) Note the cusp-like appearance. (*B*) It is quite evident that the mucosal elevations are distinct from the adjacent gastric rugae. Both patients had typical lower esophageal rings.

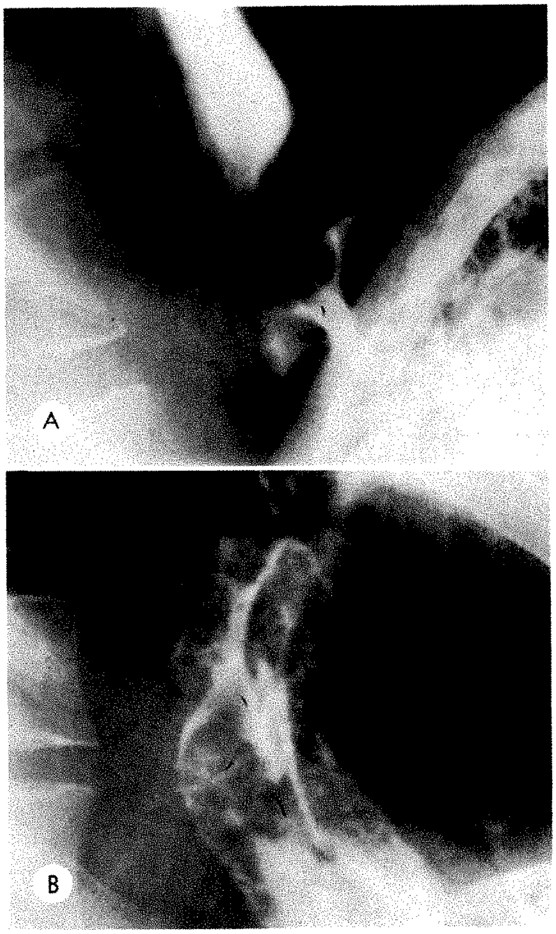


Fig. 6. A third example of mucosal redundancy in a patient with a ring. (*A*) Severe gastritis in herniated portion of stomach. The appearance suggests an ulcer crater surrounded by inflammation but actually the ulceration was in the herniated stomach (*B*).

generally higher anteriorly, one gets the false impression that the junction of the two is beneath the highest point of the diaphragm. Simply turning the patient into the lateral or steep oblique position invariably shows that the point of junction is precisely at the esophageal hiatus. When one does see a second pouch above the diaphragm and it subsequently descends below the hiatus, it simultaneously spreads out and is absorbed in the adjacent fundus and never remains tubular.

CARDIOESOPHAGEAL REFLUX

Of a related but more immediate significance is a reinterpretation of cardioesophageal reflux.

This entails a more extended discussion of the physiologic sphincter of the esophagus. The lack of any clear-cut thickening of the inner circular muscle layer at the cardioesophageal junction is the only substantial gap in the evidence of the existence of such a sphincter. On the positive side there is a considerable body of evidence. (1) It is the uniform experience of all radiologists that there is a localized constriction of the distal end of the esophagus at approximately the level of the diaphragm and slightly above it. (2) There are certain logical reasons to presume the existence of such a sphincter despite a certain gap in the morphologic evidence: (a) The muscle is there (the circular layer of the muscularis propria); (b) the circular muscle of the distal esophagus is certainly capable of contracting as a separate unit with the rest of the circular muscle of the esophagus relaxed, as indicated by the above roentgenologic evidence; (c) this area is subject to diseases of sphincters. There is a fairly perfect analogy to pyloric hypertrophy. All degrees of increased tone of the lower esophageal "sphincter" are observed and can be demonstrated fluoroscopically by the variable height at which a fluid level forms above the cardioesophageal junction when the patient swallows barium; and (d) physiologic pressure measurements[3] definitely indicate that when the remainder of the esophagus is relaxed increased pressure is observed at the cardioesophageal junction.

In refutation of arguments that there is no such sphincter, it can be said that the mere fact that there is no thickening of the circular layer of muscle of the cardioesophageal junction does not by any means rule out the possibility that the muscle in this localized region could act as a sphincter. Secondly, there is ample evidence that the diaphragm does not act as a "pinchcock." It is the opinion of a number of authors that the hiatus is simply a "hole in the diaphragm."

One often sees patients with contraction rings, hiatus hernias and clinical symptoms which indicate that cardioesophageal reflux is certainly occurring. Yet the usual maneuvers including pressure on the abdomen, Valsalva effect, etc. utterly fail to cause the sphincter to give way and permit reflux. In such cases if one gives even a small swallow of barium, as this swallow gets into the distal third of the esophagus, before it actually enters the region of the sphincter or the herniated portion of the stomach, there is a relaxation of the sphincter, evidently "triggered" by a reflex, and massive reflux from the stomach comes up to meet the swallow. If the sphincter mechanism can remain competent or nearly so above the diaphragm, there seems to be no reason to postulate that the right crus of the diaphragm plays any essential role.

It has also been proposed that the subdiaphragmatic segment of the esophagus acts as a valve in a passive fashion when the cardia balloons and presses the esophageal walls against each other. Against this conception, which admittedly has been the theoretic underpinning of much reparative surgical work about the hiatus, is the fact that it depends on the erroneous two-chamber theory, whereas there are strong doubts that there is a subdiaphragmatic esophageal segment in the first place and my own failure to find even a single genuine example of a subdiaphragmatic segment of the esophagus in a large number of cases indicates that this mechanism cannot be invoked as the normal spincter.

Without postulating any supplementary sphincter mechanism, I believe it is possible to account for all the observations in a most satisfactory way by stating that patients with esophageal shortening and hiatus hernia have cardioesophageal reflux for the same reason that patients with hemorrhoids have pruritus ani: that is, there is a simple mechanical imperfection of the valve caused by the impossibility of bringing two irregular surfaces into perfect contact as the sphincter contracts.

That such polypoid elevations exist when there is a mucosal redundancy is demonstrated above. The insufficiency might be gross enough to permit free spillage through the irregular lumen of the valve but even slight seepage into the lower third of the esophagus might well trigger the reflex mechanism which acts when fluids enter the lower third of the esophagus and causes relaxation of the physiologic sphincter and gross reflux.

If this interpretation is correct, two deductions must hold true. (1) A procedure which restored esophageal length to normal should correct the redundancy, restore the sphincter to competence and thus relieve symptoms of cardioesophageal reflux. Clinical and roentgenologic evidence on an as yet rather small group of patients indicates that this is actually the case. Indeed, in one instance the patient's symptoms were relieved even though the hiatus hernia was only partially corrected. (2) Operations aimed at correcting the hernia and "assisting" the sphincter mechanism by making the esophageal hiatus smaller are without a valid rationale and may even be harmful.

APPLICATIONS TO ESOPHAGEAL HIATUS HERNIA

Although in previous sections this condition has been touched upon as an incidental finding to another disease, there are very puzzling problems concerning esophageal hiatus hernia *per se*. On the one hand, we see patients with severe substernal distress, acid regurgitation, gastrointestinal bleeding and even profound hemorrhage, and yet these patients have rather insignificant-appearing hiatus hernias. On the other hand, one will often see as an incidental finding on a chest roentgenogram of a patient in his 70's or 80's a huge hiatus hernia with practically the entire stomach in the chest. Despite this the patients have been so asymptomatic that they have never sought medical attention for symptoms referable to the gastrointestinal tract. This has led to a rather common opinion among clinicans that the smaller the hiatus hernia, the more significant it is. Nevertheless, it is rather difficult to base rational treatment upon a paradox.

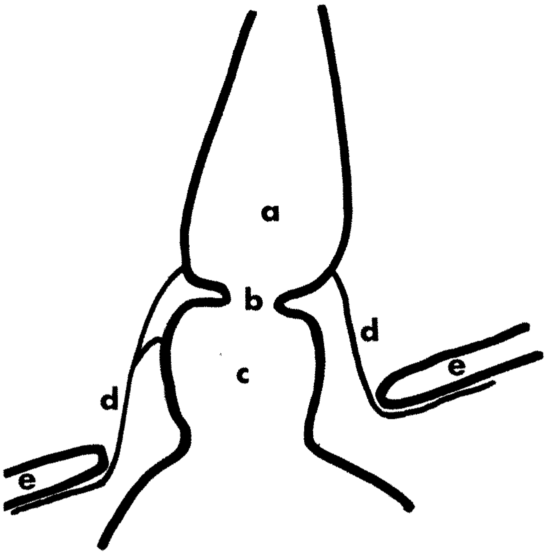


Fig. 7. Anatomy of the cardioesophageal junction (redrawn by following Sycamore[13]).

Conventional Legends	*Revised Legends*
a. Phrenic ampulla Vormagen (Luschka)	Phrenic ampulla
b. Inferior esophageal sphincter	Lower esophageal ring (mucosal plication)
c. Gastroesophageal vestibule (Lerche) Vormagen (Arnold) Cardiac antrum (Luschka) Epiphrenic bell	Hiatus hernia
d. Phrenoesophageal membrane	Phrenoesophageal membrane
e. Diaphragm	Diaphragm

The merit of the plication theory is that it places emphasis not on the hiatus hernia itself but on the effect which the hernia has on the cardioesophageal sphincter mechanism. What differentiates the symptomatic from the asymptomatic hernias is shortening of the esophagus and resulting mucosal redundancy causing reflux. The radiologist can focus his attention on the redundancy as clear and direct proof of dysfunction and has the esophageal length to assist in his evaluation. He can also test for incompetency by the usual methods and with the "trigger test" mentioned above. An evaluation of these features should assist in orientation of treatment towards correction of the basic dysfunction, *i.e.*, restoration of normal esophageal length.

ESOPHAGITIS AND ACHALASIA*

Deductions arising from an application of the plication theory to these two diseases are of a somewhat more tentative nature in view of a lack of relevant clinical and roentgenologic information. What information exists, however, neatly supports the somewhat startling hypothesis that the two are identical in origin but that some additional factor determines what the end result will be. Following the sequence indicated in Figure 8, it seems that two outcomes are possible when mucosal redundancy causes a defective valve. Either compensatory mechanisms at the cardia result in overcompensation and cardiospasm develops or a failure to compensate allows esophagitis to ensue. (There is the theoretic possibility that compensation is just right, but this is likely to be a transitory state of affairs. Similarly, a low gastric acidity may break the etiologic chain leading to esophagitis.)

There is a built-in mechanism which tends to camouflage the association of hiatus hernia with cardiospasm. When the esophagus dilates as a result of the latter, it also elongates and this, of course, brings its lower extremity back to the diaphragm. Hence, one would have no reason to suspect such an association if he considered only the classic cases of achalasia with mega-esophagus. If one is alerted to the possibility of a cross-incidence between cardiospasm and hiatus hernia, it is not hard to find cases which exhibit both. Indeed, the frequency is such that the cross-incidence could hardly be due to chance. I have not yet had an opportunity to follow a patient through progressive degrees of cardiospasm to classic mega-esophagus, nor would this be justifiable; however, it is quite possible that a search of files will permit a retrospective study of individual cases showing this progression.

To study further the factors which operate in some cases to produce hypertrophy and ganglion cell degeneration and in others fail to operate and result in esophagitis, a comparison of the clinical features of the two diseases is necessary. On the face of it, there are certain very definite differences in the types of patients who acquire the two conditions. The outstanding feature is the different age groups into which the two diseases fall. Cardiospasm is undoubtedly a disease of the elderly, whereas esophagitis occurs from infancy onward. Other factors to be investigated are the sex ratio, the gastric acidity in the two diseases, association with peptic ulcers, etc.

DISCUSSION

As far as the lower esophageal ring is concerned, the evidence seems rather complete and it is difficult to conceive of an alternate explanation being as successful. It would not be reasonable to expect that all of the extended chain of deductions from this simple but well supported hypothesis would be correct. These deductions may

---

* In this section heading I have deferred the current usage of the term *achalasia*, reserving it for severe cases of mega-esophagus even though, to the extent it means "failure to relax" (in an etiologic sense), I believe it to be incorrect. A failure to relax, were it an aganglionosis (and this seems to be implied), would be an all-or-nothing affair. On the contrary, *cardiospasm* occurs in a more or less continuous spectrum of severity and represents reality more accurately. An aganglionosis should certainly be manifested in early life as is the case with the colon and should not be affected by ganglionic blocking agents as is the case with cardiospasm.[14] Hence, there is reason to believe that the loss of ganglion cells may be degenerative (*v.i.*). At the risk of compounding the semantic confusion the question is posed: "If *achalasia* is a misnomer, is its opposite, *chalasia*, also a misnomer?"

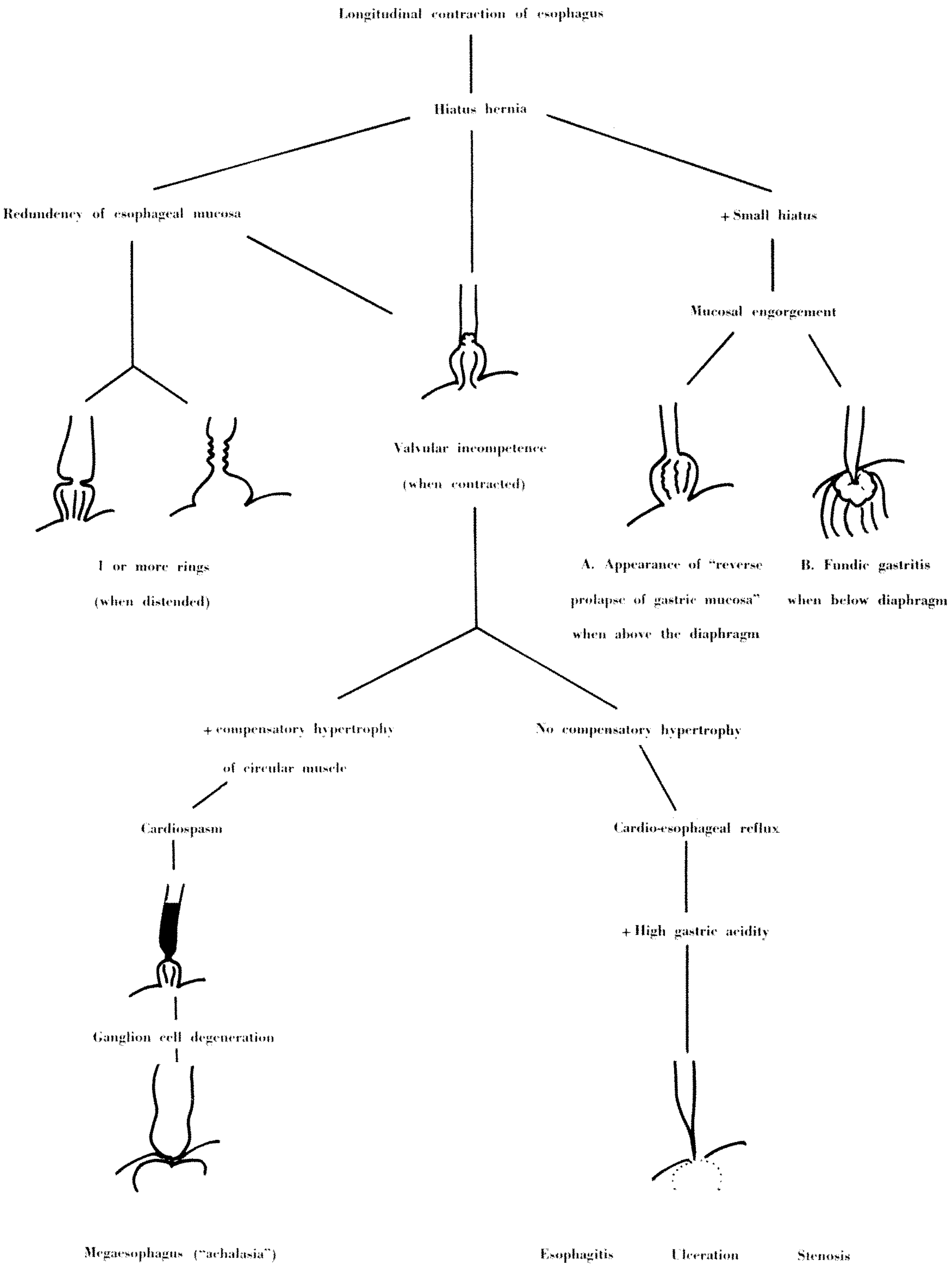


Fig. 8. Longitudinal contraction of esophagus.

well have to be revised, corrected and refined. Nevertheless, the major importance of the plication theory is the insight it gives and the stimulus it provides to direct further observations.

Its further application would lead to an investigation of all diseases of sphincters and to the evaluation of the various webs, diaphragms and partial membranes which are seen in the gastrointestinal tract. One can generalize even farther afield and seek applications to diseases affecting other hollow muscular organs, particulary the bronchi, the ureters, the urethra, and the fallopian and eustachian tubes.

SUMMARY

After a review of the salient features of the lower esophageal ring, a mechanism is proposed which gives a reasonable account of the condition. The further implications of this mechanism are explored.

110 East Main Street
Madison, Wisconsin

REFERENCES

1. de Lorimier, A. A., and Warren, J. P. Prolapse of mucosa at esophagogastric junction. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1960, *84*, 1061–1069.
2. Gary, J. E., and Schatzki, R. Radiologic examination of gastrointestinal tract. *New England J. Med.*, 1954, *251*, 1052–1058.
3. Harris, L., Kelly, J. E., Jr., and Kramer, P. Relation of lower esophageal ring to esophagogastric junction. *New England J. Med.*, 1960, *263*, 1232–1235.
4. Ingelfinger, F. J., and Kramer, P. Dysphagia produced by contractile ring in lower esophagus. *Gastroenterology*, 1953, *23*, 419–430.
5. Kramer, P. Frequency of asymptomatic lower esophageal contractile ring. *New England J. Med.*, 1956, *254*, 692–694.
6. Lerche, W. The Esophagus and Pharynx in Action: A Study of Structure in Relation to Function. Charles C Thomas, Publisher, Springfield, Ill., 1950.
7. MacMahon, H. E., Schatzki, R., and Gary, J. E. Pathology of lower esophageal ring; report of case, with autopsy, observed for nine years. *New England J. Med.*, 1958, *259*, 1–8.
8. Nissen, R. Repair of esophageal hiatal hernia by fixation to anterior abdominal wall. In: Current Surgical Management. II. J. H. Mulholland, editor, W. B. Saunders Company, Philadelphia, 1960.
9. Schatzki, R., and Gary, J. E. Dysphagia due to diaphragm-like localized narrowing in lower esophagus ("lower esophageal ring"). Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1953, *70*, 911–922.
10. Schatzki, R., and Gary, J. E. Lower esophageal ring. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1956, *75*, 246–261.
11. Schumacher, S. Handbuch der Microskopischen Anatomie des Menschen. J. Springer Verlag, Berlin, 1927.
12. Stiennon, O. A. Prolapse of antral mucosa; clinical-radiologic entity? Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1960, *84*, 1142–1143.
13. Sycamore, L. K. Radiologic diagnosis of hiatus hernia. *Gastroenterology*, 1956, *31*, 169–189.
14. Wright, J. T. Buscopan and oesophageal achalasia. *Brit. J. Radiol.*, 1961, *34*, 113–119.
15. Zaino, C., Poppel, M. H., Jacobson, H. G., Lepow, H., and Osturk, C. H. Lower esophageal vestibular complex; anatomic-roentgen study. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1960, *84*, 1045–1055.

◆

PHARYNGEAL CINEFLUOROGRAPHY IN CLINICAL PRACTICE*

By JAMES H. SCATLIFF, M.D.,† *and* M. PETER SCIBETTA, M.D.‡
NEW HAVEN, CONNECTICUT

ACCURATE fluoroscopic evaluation of a barium bolus which is rapidly accelerated from a standing position to a speed of approximately 2 feet per second as it moves through a 5 inch long tube is almost totally impossible. Spot filming methods including a preliminary "count down" of the swallowing process, palpation of the upward moving thyroid cartilage or radiation timed exposures[5] can at times provide considerable roentgenographic data.

We have found in the last several years, however, that the substitution of cinefluorographic methods for spot roentgenographic techniques is a practical and important means of pharyngeal assessment. Examination may be carried out in multiple projections with a small number of barium swallows. The examination is accomplished quickly for both patient and radiologist. For a minimal sacrifice in roentgenographic detail, abundant information is obtained which may be analyzed in slow motion and single frames.

The majority of reports in the past concerning cinefluorography of the pharynx have been related to the study of normal or abnormal swallowing mechanisms, including the pathophysiology of the cricopharyngeus muscle.[1,2] The purpose of this communication is to emphasize the value of cinefluorographic techniques as a highly accurate yet simple routine in the evaluation of extrinsic and intrinsic pharyngeal lesions as well as to present illustrative cases.

EQUIPMENT

The 5 inch Philip Image Intensifier was used in all studies. Although a 5 inch image amplifier field is somewhat limited, the greater ratio of the area of interest to the cine frame space improves upon detail obtained. The majority of examinations were carried out with a 35 mm. Arriflex camera and Kodak Cineflure film. Processing was done with an Oscar Fisher Process-All using Eastman Rapid Liquid X-ray developer. Film strips averaging 75–100 feet in length were viewed with a Tage-Arno projector.

EXTRINSIC LESIONS

I. PARATHYROID ADENOMA

Case i. A.E. N.H.U. No. B 98822. This 30 year old white female had a 9 year history of right renal colic, calculi, and repeated urinary tract infections which necessitated a right nephrectomy in July, 1961. Significant laboratory findings included a serum calcium of 13.0 mg. per cent and 15.5 mg. per cent; phosphorus 1.6 mg. per cent and 1.5 mg. per cent. Physical examination at this time revealed a 1.5 cm. nodule over the right lower thyroid. Roentgenographic survey showed a small left renal calculus, generalized demineralization and a fine mottled pattern of the skull and bones of the distal forearm. Cinefluorography demonstrated an abnormal indentation of the right posterolateral hypopharynx (Fig. 1, *A*, *B* and *C*). Operation on July 25, 1961 revealed an adenomatous parathyroid nodule at the approximate level noted in the cinefluorogram. The specimen measured 2×2.5×1 cm. and weighed 160 mg.

The patient did not experience satisfactory symptomatic improvement postoperatively and 4 months later abnormal calcium and phosphorus findings (calcium 12.5 mg. per cent, phosphorus 2.1 mg. per cent) were again noted. The patient thought that she had a mass in the left thyroid area. Although it could not be palpated definitely at this time, one month later it became well defined. A repeat cine study of the esophagus and pharynx was then performed (Fig. 1, *D*, *E* and *F*). Exploration of the left side on January 5, 1962 revealed a second parathyroid adenoma in the region of the inferior pole of the left lobe of the thyroid. The adenoma weighed 1 gm. and measured 1.5×2 cm. Since this operation the chemical studies have become normal and the patient has remained asymptomatic.

---

* From the Department of Radiology, Yale University School of Medicine and Radiology Service, Grace-New Haven Community Hospital, New Haven, Connecticut.

Presented at the Tenth Annual Meeting of the Association of University Radiologists, Indianapolis, Indiana, May 20, 1962.

† Assistant Professor, Department of Radiology, Yale University School of Medicine.

‡ Instructor, Department of Radiology, Yale University School of Medicine.

Case II. J.S. N.H.U. No. A 4428. This 65 year old white female underwent pyelolithotomy 10 years before the present admission. Hypercalcemia (13.8 mg. per cent) was documented at that time. Hyperparathyroidism was suggested but surgical exploration was not carried out. In the following 10 years, the patient experienced vague intermittent back pain, excessive fatigue, and constipation. On admission to the Grace-New Haven Hospital in 1961 she gave a 3 day history of an acute onset of nausea and vomiting accompanied by severe pain in the left neck and shoulder. Palpation of the neck on the left side revealed a 1.5 cm. nodule in the region of the lower pole of the left lobe of the thyroid. Laboratory examination showed a serum calcium of 12.7 mg. per cent and phosphorus of 3.5 mg. per cent. Roentgenograms demonstrated changes in the skeleton compatible with hyperparathyroidism. These included generalized demineralization of the bones and cystic and subperiosteal bone resorption in both hands and feet. Left renal calculi were noted. Cinefluorograms indicated the presence of a large adenoma on the left (Fig. 2*A*). Operation revealed a 5×3×2

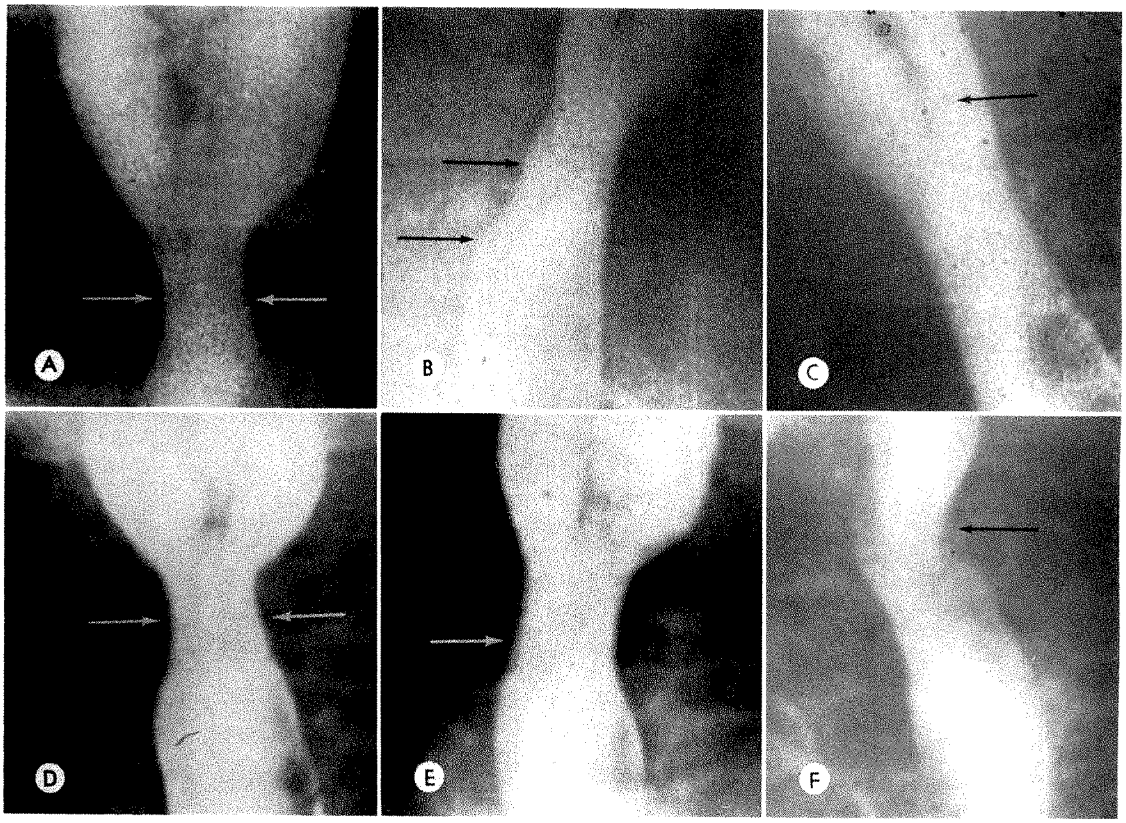


Fig. 1. Case 1. Asynchronous development of parathyroid adenomas. (*A*) Moderate asymmetry in cricopharyngeal region (arrows) is seen without localization of adenoma. (*B*) Left posterior oblique projection brings out indentation (between arrows) by adenoma on right posterolateral wall of hypopharynx. (*C*) Right posterior oblique projection shows normal outline of left posterolateral wall of hypopharynx. Arrow indicates inferior aspect of left pyriform sinus. (*D*) Second examination 6 months after first exploration shows minimal asymmetry in the anteroposterior projection. (*E*) Left posterior oblique projection (less obliquity than in *B*) shows normal right posterolateral wall of hypopharynx. (*F*) Right posterior oblique projection. Arrow denotes constant defect due to second parathyroid adenoma not defined in first study.

cm. parathyroid adenoma weighing approximately 12.5 gm. (Fig. 2*B*).

Comment. Precise roentgenographic localization of parathyroid tumors has come from two directions. Wyman and Robbins[10] stressed the importance of spot roentgenography of pharyngeal and esophageal parathyroid indentations in 1954. In a series of 34 cases of parathyroid adenomas removed at surgery, roentgen localization was obtained in 20. Although tracheal indentation alone served to identify several tumors, the majority of lesions produced esophageal defects with or without tracheal compression. Of significance also is the fact that almost all of the esophageal indentations were approximately an inch or greater (2 cm. through 7 cm., measured in a vertical plane). This would suggest that defects in the pharynx or esophagus made by smaller adjacent lesions could not be recognized, or recognized with certainty, with this method.

A second roentgenographic approach has been angiographic localization by way of retrograde catheterization of the subclavian artery. Roentgenographic confirmation of displacement of the inferior thyroid artery and its branches was used by Seldinger[8] to define lesions as small as 1 cm.×2 cm. The technique would appear to be particularly useful when an adenoma has migrated to the anterior mediastinum away from the esophagus. For complete evaluation of the parathryoid structures, however, bilateral brachial punctures and catheterization were required, a step which may not be justified in the face of negative information and the danger involved in arteriosclerotic age groups.

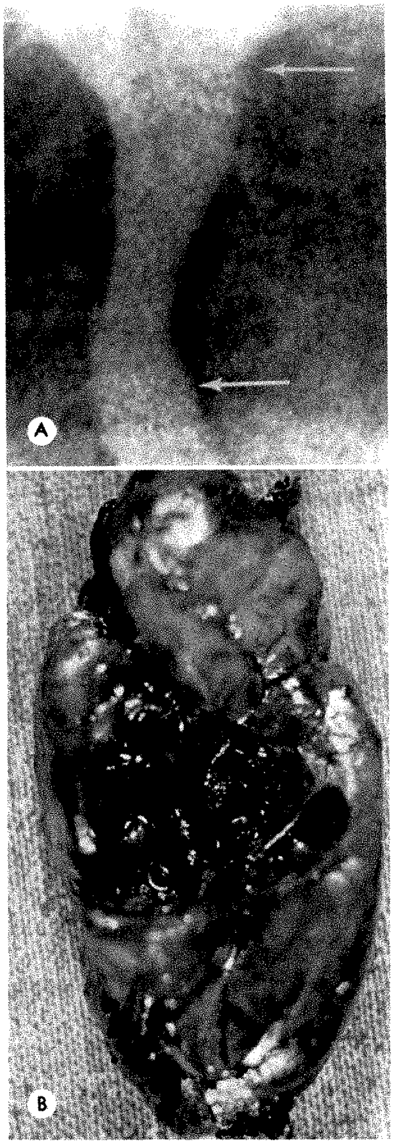
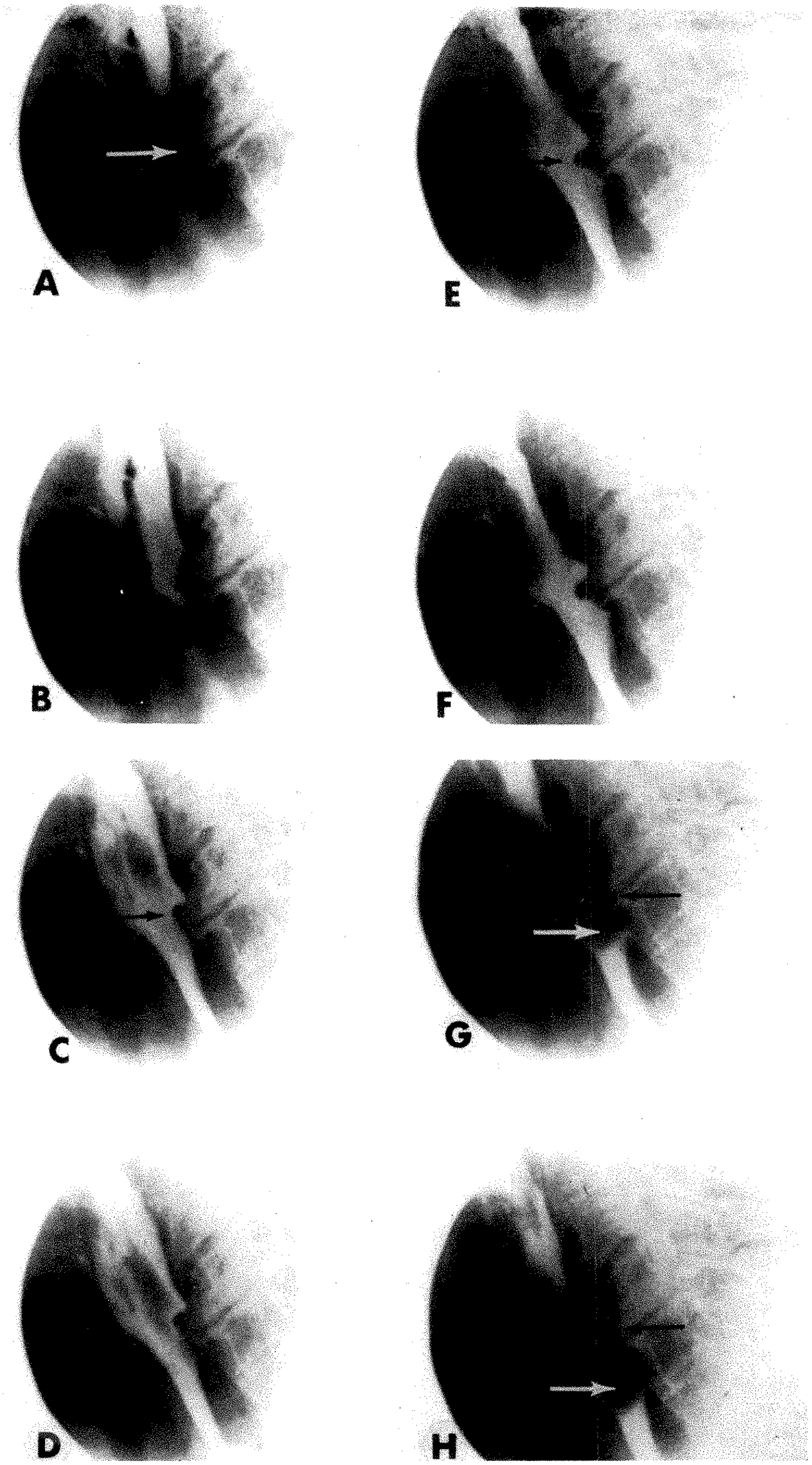


Fig. 2. Case II. Large parathyroid adenoma. (*A*) Upper arrow indicates defect at inferior aspect of left pyriform sinus due to adenoma. Lower arrow is at approximate inferior edge of lesion. (*B*) Specimen is 5×3×2 cm. Weight 12.5 gm.

The 2 cases reported underscore the virtues of cinefluorography in detecting both minimal pharyngeal defects as well as in documenting the extent of larger lesions. Case I is important in bringing out the value of filming the pharynx in oblique planes as well as in anteroposterior and lateral projections. Without oblique views of this patient, the moderate asymmetry of the cricopharyngeal region seen in the anteroposterior projection could have been regarded as having only questionable significance. The cinefluorographic appreciation of definite compression of the inferior aspect of the left pyriform sinus helped localize a relatively large lesion indenting the left cricopharyngeal region and not the right.

It is obvious that the small adenoma


A
E
B
F
C
G
D
H

situated on the posterolateral aspect of the thyroid or displaced into the anterior mediastinum will not make itself known cinefluorographically. Modern surgical practice, however, employs complete investigations of the parathyroids in the neck or mediastinum in the presence of clinical and laboratory evidence of hyperparathyroidism. Cinefluorography can very often point the way to the enlarged gland, leading to a more rapid and confident surgical exploration.

2. OSTEOPHYTE DYSPHAGIA[4]

Case III. G.K. N.H.U. No. 857039. This 85 year old male was admitted to the Grace-New Haven Hospital complaining of pain in the throat, increasing dysphagia for several months and a weight loss of 30 lb. Roentgenograms of the cervical spine showed a prominent osteophyte at C5–C6. Direct laryngoscopy was normal. Esophagoscopy revealed a markedly edematous posterior hypopharyngeal wall immediately above the cricopharyngeus. Cinefluorography as carried out and interpreted is shown in Figure 3, *A–H*. Surgical excision of the osteophyte was performed with subsequent improvement in swallowing function.

Comment. Osteophyte indentation of the posterior hypopharynx, particularly in the aged, is a not uncommon roentgenographic finding. Many of these patients do not appear, however, to have symptoms related to osteophyte intrusion. Swallowing is either accomplished normally or with moderate disability secondary to neuromuscular dysphagia. Presurgical confirmation, therefore, of osteophyte dysphagia is especially important in older age groups.

Case III illustrates the value of careful frame by frame analysis. The osteophyte at the C5–C6 level made an obvious defect in the barium column. On the other hand, liquid barium passed over the osteophyte without delay and only moderate slowing of thick barium was noted. The suggestion that the cricopharyngeous sustained repeated irritation as it was drawn up aginst the osteophyte during deglutition could only be made after cine study.

INTRINSIC DEFECTS

I. PLUMMER-VINSON WEBS

Case IV. J.J. N.H.U. No. B 11881. This 52 year old white female presented with a 14 year history of weakness and a recent onset of mild dysphagia with a sensation of food sticking at the level of the lower neck. Laboratory examination established the presence of an iron deficiency anemia (hematocrit 26 per cent, serum iron 30 μg. per cent). Cinefluorography (Fig. 4, *A* and *B*) and esophagoscopy demonstrated a Plummer-Vinson web. The patient's symptoms have improved following iron therapy.

Comment. In 1939 Waldenström and Kjellberg[9] published the classic roentgenographic description of the Plummer-Vinson web. These authors using short exposure (.03–.05 seconds) spot roentgenograms demonstrated web formation, particularly in the lateral view. Roentgenography was accurate enough to distinguish the horizontal as well as vertical length of the web, multiple webs, and fine mucosal folds unrelated to the Plummer-Vinson abnormality.

In order to achieve satisfactory results

←

Fig. 3. Case III. Serial cinefluorograms (24 per second) suggesting cricopharyngeal irritation by osteophyte at C5–C6 level. Total period between frame *A* and *H* is $\frac{3}{8}$ seconds. (*A*) Barium column immediately above osteophyte (arrow). (*B*) One twenty-fourth second later barium is deflected by osteophyte. (*C* and *D*) Rounded defect begins to form in barium column immediately anterior to osteophyte (arrow) 1/12 second after frame *B*. New defect represents beginning contraction of cricopharyngeus muscle. (*E* and *F*) One-twelfth second after frame *D* cricopharyngeal shadow becomes more prominent (arrow). (*G* and *H*) One-sixth second after frame *F* cricopharyngeus moves below osteophyte. Arrow on the right in each frame denotes osteophyte; arrow on the left indicates cricopharyngeus.

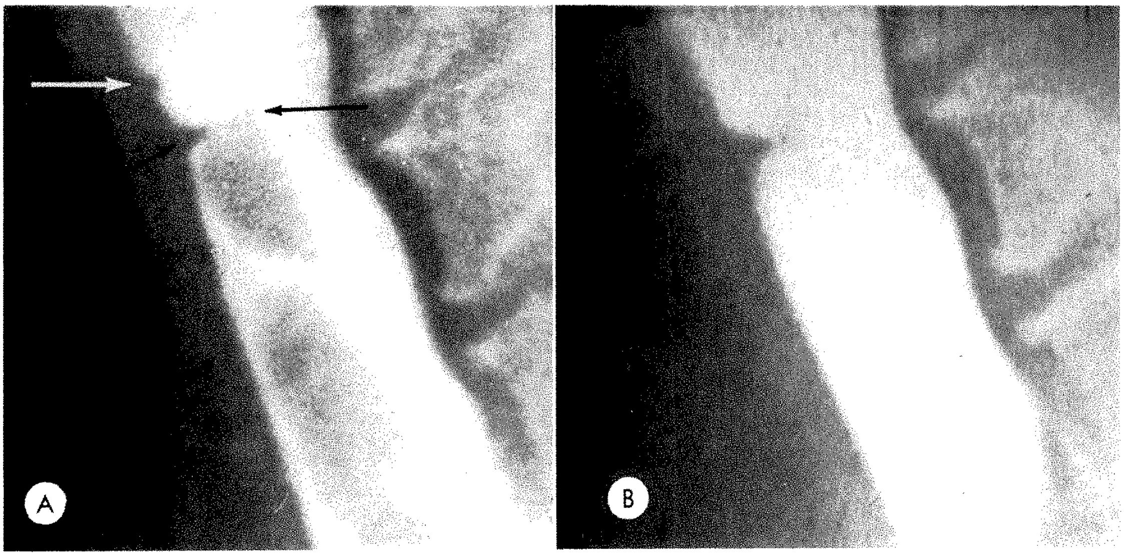


FIG. 4. Case IV. (*A*) Plummer-Vinson web (between arrows) is outlined by thin barium and air column below web. Single arrow points toward smaller web. (*B*) Thick barium partially obscures larger web. Smaller web is indistinctly seen.

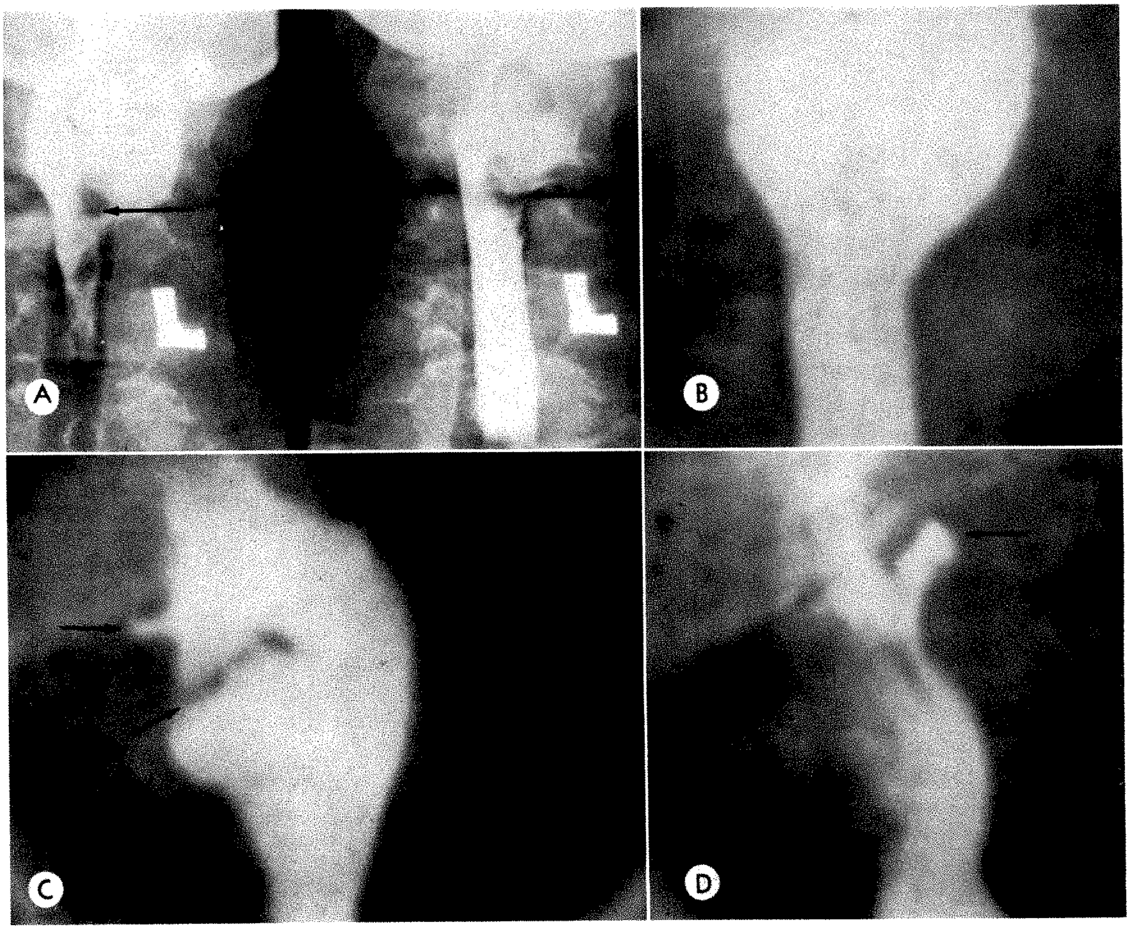


FIG. 5. Case V. (*A*) Thick barium and spot roentgenograms show questionable lesion at inferior aspect of left pyriform sinus (arrows). (*B*) Cinefluorogram with thin barium in anteroposterior projection shows no evi-

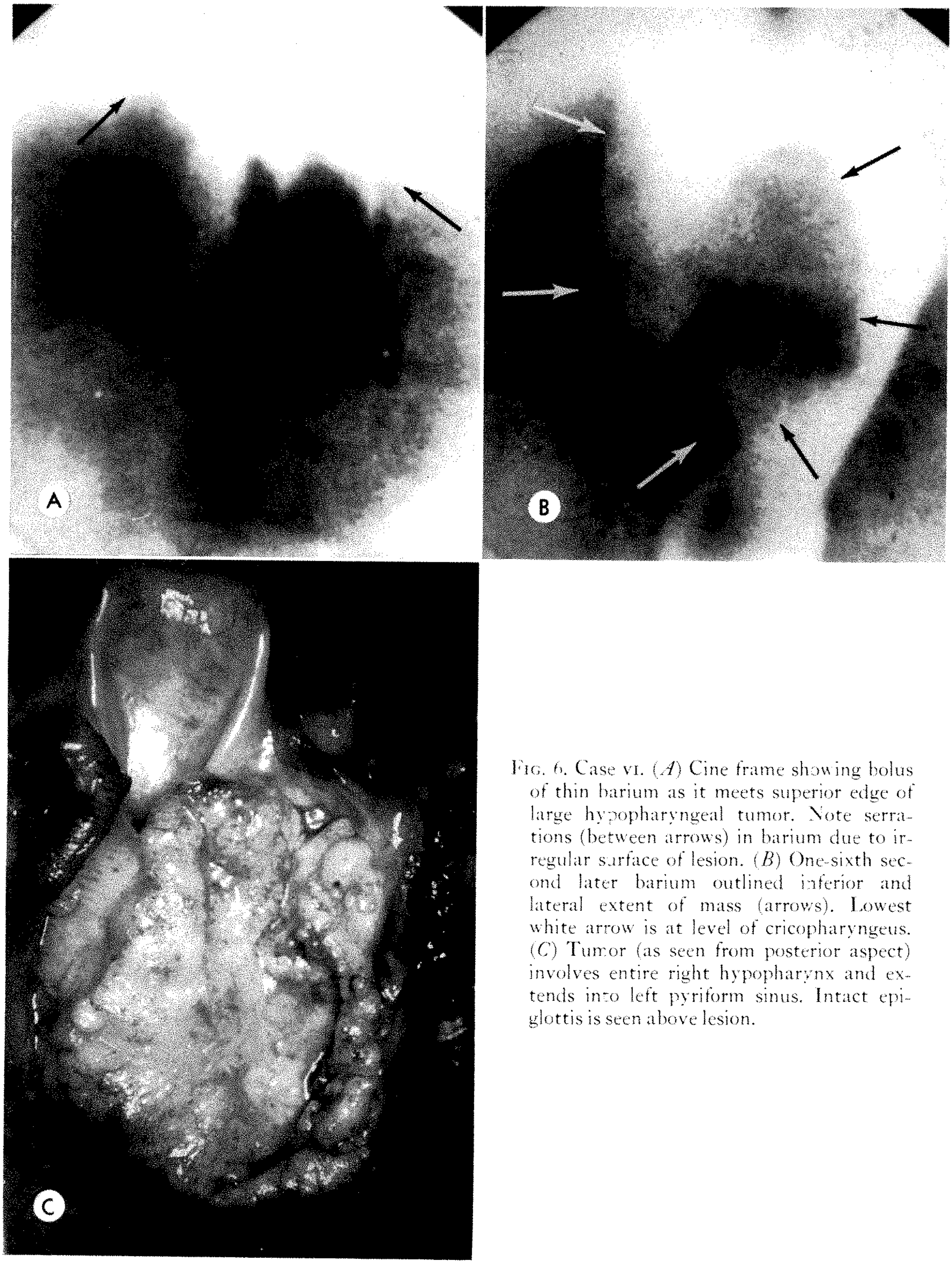


Fig. 6. Case vi. (*A*) Cine frame showing bolus of thin barium as it meets superior edge of large hypopharyngeal tumor. Note serrations (between arrows) in barium due to irregular surface of lesion. (*B*) One-sixth second later barium outlined inferior and lateral extent of mass (arrows). Lowest white arrow is at level of cricopharyngeus. (*C*) Tumor (as seen from posterior aspect) involves entire right hypopharynx and extends into left pyriform sinus. Intact epiglottis is seen above lesion.

---

dence of defect. (*C*) Right posterior oblique projection also reveals a normal left pyriform sinus. Upper arrow denotes lateral pharyngeal diverticulum on the right. Lower arrow indicates epiglottis. (*D*) Maximum filling of left lateral pharyngeal diverticulum (arrow) is obtained as pharynx contracts and barium bolus moves into esophagus.

the "count down" film exposure method was employed; the patient swallowed a thick barium paste and a roentgenogram was made at a pretested number. Since that time, thick mixtures of barium have generally been recommended to reduce the flow rate of contrast material in the hypopharynx for adequate filming. The thicker bolus was also used to produce maximum distention of the cricopharyngeal area in order to enhance recognition of the web.

Cinefluorography as illustrated by Case IV provides the additional advantage of the use of thin barium mixtures. Although air-barium contrast about the web in this case is unusual, thin mixtures appear to give a clearer view of the defect than heavier barium preparations (Fig. 4, *A* and *B*). As in the case of parathyroid adenoma indentations of the pharynx, oblique filming of the web can be utilized to better assess the dimensions of the web. Cine studies will outline the usual downward inclination of the fine mucosal fold described by Waldenström and Kjellberg in contrast to the horizontal plane occupied by the Plummer-Vinson web.

2. CARCINOMA OF THE HYPOPHARYNX

Case v. V.D. N.H.U. No. 57-21-23. This 46 year old female had a long history of multiple complaints which had been attributed to a severe psychoneurosis. The patient was examined by the Otolaryngology Service for a 6 month history of hoarseness. Barium spot roentgenograms suggested the presence of a lesion in the left pyriform sinus (Fig. 5*A*). Endoscopic examination revealed minimal edema of the vocal cords. No defect could be demonstrated in the pyriform sinuses. Cinefluorograms as shown in Figure 5, *B–D* showed no evidence of a mass in the left pyriform sinus.

Case vi. V.P. N.H.U. No. 54-08-046. This 80 year old white male entered the Grace-New Haven Hospital with a 2 week history of dysphagia and a painless lump in the right neck for one month. There had been blood-tinged saliva and some hoarseness. Oropharyngeal inspection revealed a large pyriform sinus carcinoma. Endoscopy indicated that the tumor extended from the right pyriform sinus to the medial wall of the left pyriform sinus. The inferior margin of the mass could not be ascertained and cinefluorography was done with the results shown in Figure 6, *A*, *B* and *C*. Total laryngectomy and right radical neck dissection were performed. The histologic report was epidermoid carcinoma.

Case vii. J.A. N.H.U. No. C 20428. This 57 year old white male was seen in March, 1961 with pain in the throat and some bloody saliva of one month's duration. He had noted a gradually enlarging mass in the right neck for several months. Physical examination revealed large lymph nodes in the neck. Inspection of the oropharynx showed medial displacement of the right tonsil by a golf ball-sized, firm mass. The tumor extended from this level to the right pyriform sinus as well as the right aryepiglottic fold. Cinefluorography (Fig. 7, *A*, *B* and *C*) and endoscopic examination showed a large 2.5 cm. in diameter ulcer on the posterior wall of the hypopharynx. A lesion of the soft palate was noted. Biopsy of this lesion and the oral tumor was positive for epidermoid carcinoma. There was immediate response to radiation, but the tumor reappeared shortly thereafter with subsequent hemorrhage and death.

Case viii. C.K.C. N.H.U. No. 51-90-69. This 59 year old white male entered the Grace-New Haven Hospital in March of 1960 because of burning and dryness in the throat for 3 months associated with progressive hoarseness, dysphagia and weight loss. Physical examination revealed a 1.2 cm. lesion of the right aryepiglottic fold extending into the right pyriform fossa. Cinefluorograms (Fig. 8, *A* and *B*) showed tumor infiltration of the lateral and medial aspect of the right pyriform sinus adjacent to the right aryepiglottic fold. The vocal cords and subglottic region appeared normal and a tumor mass was present in the right aryepiglottic fold. Hemilaryngectomy was performed, and the findings confirmed (Fig. 8*C*).

Comment. Cinefluorography can play a valuable complementary role in the examination or exclusion of hypopharyngeal tumors. Endoscopy with accompanying biopsy is usually the best means of appraisal of lesions in this region. Cinefluorography with opaque materials prior to endoscopy, however, may be used as a preliminary guide for thorough direct study

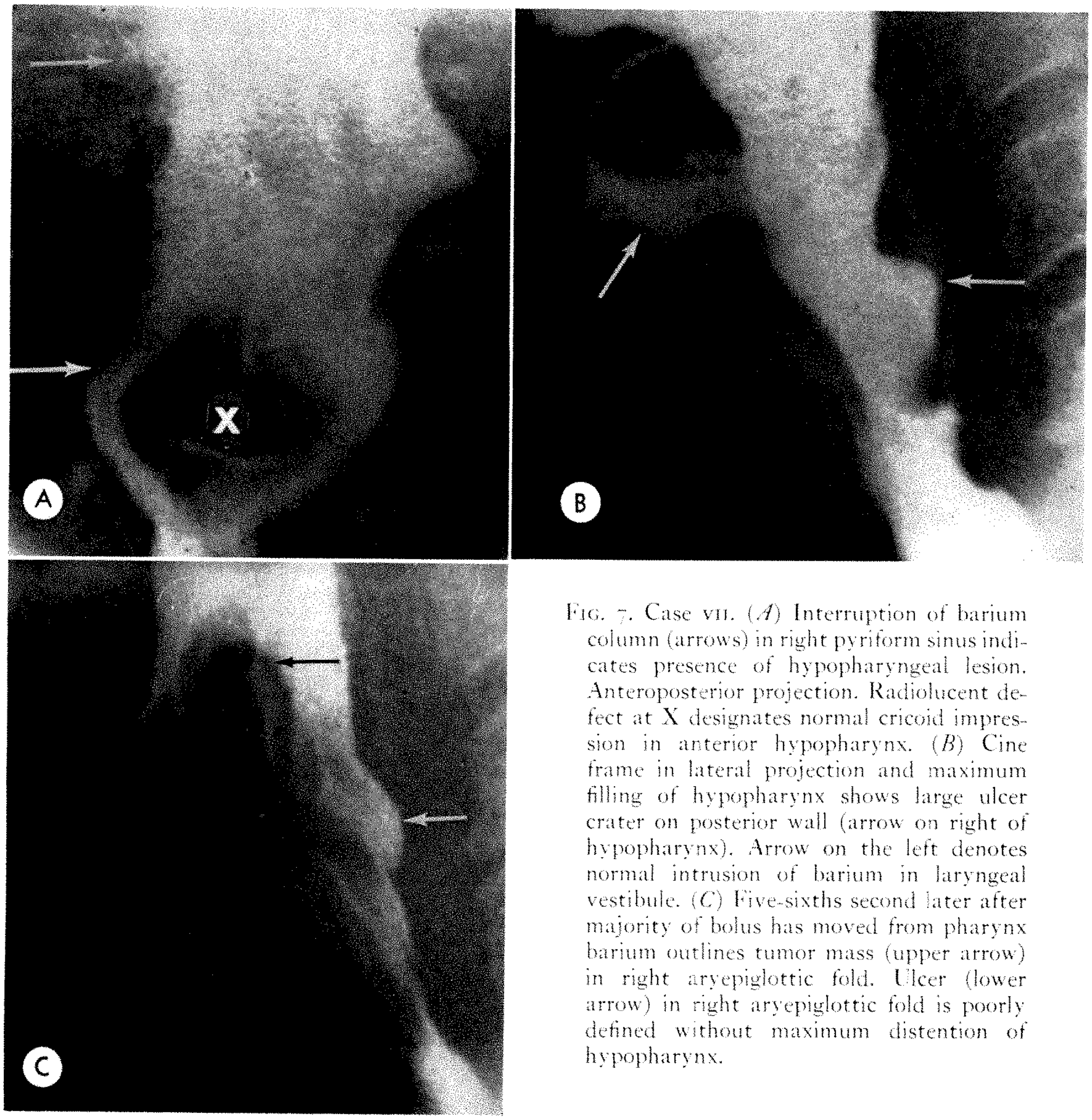


Fig. 7. Case vii. (*A*) Interruption of barium column (arrows) in right pyriform sinus indicates presence of hypopharyngeal lesion. Anteroposterior projection. Radiolucent defect at X designates normal cricoid impression in anterior hypopharynx. (*B*) Cine frame in lateral projection and maximum filling of hypopharynx shows large ulcer crater on posterior wall (arrow on right of hypopharynx). Arrow on the left denotes normal intrusion of barium in laryngeal vestibule. (*C*) Five-sixths second later after majority of bolus has moved from pharynx barium outlines tumor mass (upper arrow) in right aryepiglottic fold. Ulcer (lower arrow) in right aryepiglottic fold is poorly defined without maximum distention of hypopharynx.

of both the pharynx and larynx. The large lesion (Case vi) or a lesion with ill-defined margins and ulceration (Case vii) can be mapped out in several planes with the cine method.

This approach is particularly useful in defining the inferior and lateral margins of an exophytic hypopharyngeal lesion in areas which may not come into adequate endoscopic view because of the size or disposition of the lesion to bleed. Small infiltrative lesions deep in the pyriform sinus as in Case viii or shallow tumors on the postcricoid pharyngeal surface have been discovered only by cinefluorographic techniques. Localized edema, however, may produce the same alteration in the barium outline of the hypopharyngeal wall and exact diagnosis of defects of this kind must be made by endoscopy and biopsy.

The instillation of a bronchographic medium in the larynx as in Case viii has been suggested by several investigators for evaluation of tumors of this structure.[3,7] This technique coupled with cinefluorography can give further documentation of

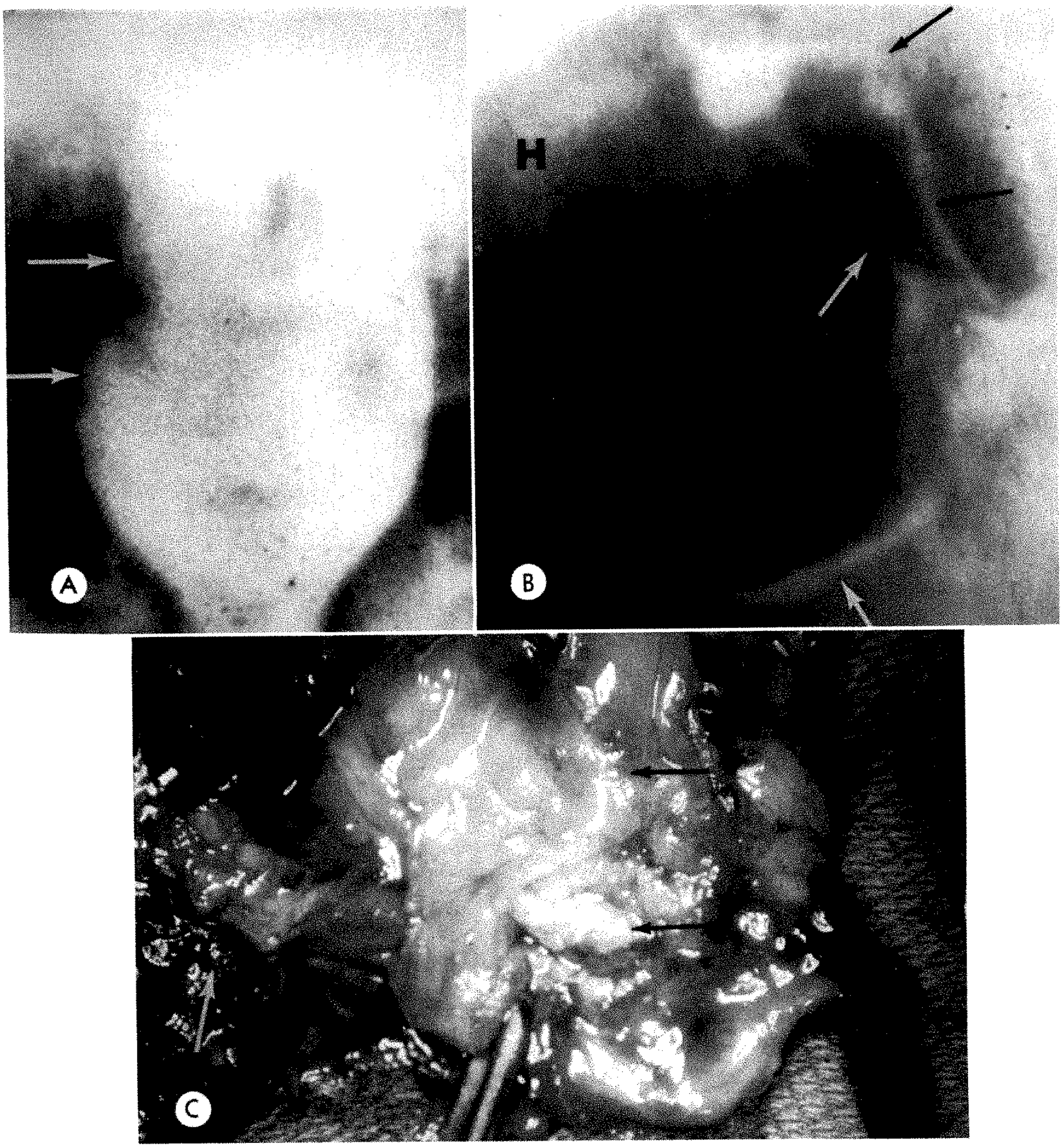


Fig. 8. Case viii. (*A*) Irregular margin of lateral aspect of right pyriform sinus (arrows) indicates presence and inferior extent of tumor. (*B*) Cine laryngogram shows distorted right aryepiglottic fold due to tumor (black arrows). Upper white arrow points to normal left aryepiglottic fold. Lateral projection. Hyoid bone at *H*. Lower white arrow denotes contrast material in normal laryngeal ventricles. (*C*) Hemilaryngectomy specimen includes right hypopharynx (between forceps) and tissue excised during right radical neck dissection (arrow on the left). Lower arrow on the right points to tumor in right pyriform sinus. Upper arrow denotes tumor mass in right aryepiglottic fold.

hypopharyngeal lesions arising in or spreading to the larynx.[6]

RADIATION EXPOSURE

The development of image intensifiers has permitted apparently safe radiation levels for cinefluorographic examinations of many different body areas. Although exact measurements are difficult to obtain, the approximate skin dose in the region of the posterior neck during a 100 foot 35 mm. film study has been 9–10 r. The values were obtained using a Victoreen chamber and a pressdwood phantom simulating an anteroposterior neck diameter of 15 cm. The exposure factors (3 phase generator) have been 75–80 kv. at 30 ma. In contrast to this, 8 spot roentgenograms, 4 anteroposterior and 4 lateral, of the neck with barium produce a skin dose of approximately 3 r. Although there is a difference in radiation levels between the two methods in favor of spot roentgenography, the great increase in information obtained as well as the rapidity of performing the cinefluorographic study outweigh the moderate increase in exposure to the patient in the cine approach.

REPRODUCTION OF CINE FRAMES

One of the current limitations of cinefluorography is transmission of information in single frames to a lecture audience or preparation of frames for publication. The cine frame may be enlarged directly on photographic print as shown in Figure 3, *A–H*. This process, however, is time consuming for the amateur radiologist-photographer as well as the professional layman. The apparatus shown in Figure 9 has proven quite helpful in obtaining rapid and detailed cinefluorographic reproductions for slide projection or prints.

If slides are desired a 35 mm. direct positive film is used. Prints can be made on any good fine grain black and white film. The cine projector may be stopped at the frame required and projected on the rear projection screen.* Particular areas of interest in the cine frames such as the Plummer-Vinson web (Fig. 4, *A* and *B*) can be photographed by moving the camera tripod closer to the screen. Sample exposure factors for an image of normal intensity are f 3.5-f 5.6; 1–4 seconds; using fine grain black and white film with an ASA rating of 40. Single lens reflex camera with an f 2.8–40 mm. lens is used.

SUMMARY

Cinefluorography can play an important role in the diagnosis or confirmation of extrinsic and intrinsic hypopharyngeal lesions. For a modest sacrifice in film detail an abundant quantity of roentgenographic information is obtained regarding the size, extent and effect on normal deglutition of various lesions. The examination may be carried out rapidly in multiple projections including oblique views. The use of rear projection screens is recommended for improved and time saving photographic reproduction of single cinefluorographic frames.

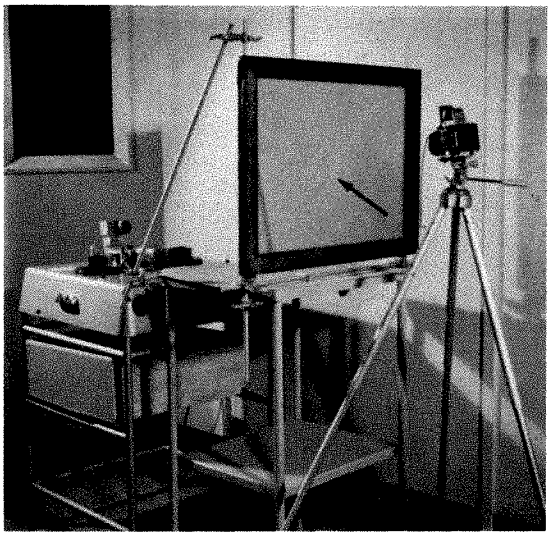


Fig. 9 Thirty-five millimeter cine projector on the left with cover removed. Image is thrown on rear projection screen (arrow). Single lens reflex camera on tripod on right can be moved for full or close-up view of cine image.

James H. Scatliff, M.D.
Department of Radiology
Yale University School of Medicine
and Radiology Service
Grace-New Haven Community Hospital
789 Howard Avenue
New Haven 4, Connecticut

REFERENCES

1. Crichlow, T. V. L. Cricopharyngeus in radiography and cineradiography. *Brit. J. Radiol.*, 1956, *29*, 546–556.
2. Dohlman, G., and Mattison, O. Role of cricopharyngeal muscle in cases of hypopharyngeal diverticula: cineroentgenographic study. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *81*, 561–569.

---

* Made by Polacoat, Inc., Blue Ash, Ohio.

3. Fabrikant, J. I., Richards, G. J., Jr., Tucker, G. F., Jr., and Dickson, R. J. Contrast laryngography in evaluation of laryngeal neoplasms. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *87*, 822–835.
4. Hilding, D. A., and Tachdjian, M. O. Dysphagia and hypertrophic spurring of cervical spine. *New England J. Med.*, 1960, *263*, 11–14.
5. Hughes, D., and Wood, M. Instrumental and technical notes: x-ray set triggering for barium swallow radiographs. *Brit. J. Radiol.*, 1959, *32*, 699–700.
6. Kirchner, J. A., Scatliff, J. H., and Shedd, D. P. Cinefluorography in pre- and post-operative management of laryngeal cancer. *Ann. Otol., Rhin. & Laryng.*, 1960, *69*, 768–780.
7. Powers, W. E., McGee, H. H., Jr., and Seaman, W. B. Contrast examination of larynx and pharynx. *Radiology*, 1957, *68*, 169–178.
8. Seldinger, S. I. Localization of parathyroid adenomata by arteriography. *Acta radiol.*, 1954, *42*, 353–366.
9. Waldenström, J., and Kjellberg, S. R. Roentgenological diagnosis of sideropenic dysphagia: Plummer-Vinson's syndrome. *Acta radiol.*, 1939, *20*, 618–638.
10. Wyman, S. M., and Robbins, L. L. Roentgen recognition of parathyroid adenoma. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1954, *71*, 777–784.

INTERNAL BILIARY TRACT FISTULAE*

By C. JULES ROMINGER, M.D., and CHRISTOPHER W. CANINO, M.D.
PHILADELPHIA, PENNSYLVANIA

FISTULAE of the biliary tract, while being of considerable interest from a roentgenologic, medical and surgical standpoint, have been infrequently reported. The roentgenographic features are often spectacular. It is our purpose to review the roentgenographic features of biliary tract fistulae and discuss 16 additional cases observed in the last decade by us.

As pointed out by Shehadi,[3,4] the diagnosis of biliary fistula was usually made on the operating table or at autopsy before the discovery and application of the roentgen ray. Arango and Marmolejo[1] reviewed the literature up to 1950. Since then only a few papers on this subject have appeared in the radiologic literature. Shehadi[4] found a total of 193 cases reported in the English language literature and added 11 of his own for a total of 204 cases.

CLINICAL FEATURES

The incidence of spontaneous internal bilary tract fistulae after Courvoisier (366 cases) as referred to by Arango and Marmolejo is given in Table I.

TABLE I

INTERNAL BILIARY TRACT FISTULAE (SPONTANEOUS)

	No. of Cases	Per Cent
Cholangioduodenal	123	33.6
Cholecystoduodenal	93	25.4
Cholangiocolic	50	13.7
Cholecystocolic	49	13.6
Cholangiogastric	10	2.7
Cholangiothoracic	10	2.7
Cholecystogastric	8	2.1
Biliobiliary	8	2.1
Biliourinary	6	1.6
Hepatogastric	4	1.1
Bilioretroperitoneal	4	1.1
Cholecystojejunal	1	0.3

In our series the distribution of anatomically connected structures was as follows: cholecystoduodenal, 6; cholecystocolic, 3; choledochoduodenal, 5; cholecys-

TABLE II

INTERNAL BILIARY TRACT FISTULAE (POSTOPERATIVE)

Patient, Age and Sex	Type	Symptoms	Physical Examination	Roentgenographic Findings	Operation
J.G. 66-M	Cholecystojejunal	Anorexia, weight loss, dark urine, clay colored stools	Jaundice	First gastrointestinal study: Irregularity of medial margin of duodenum. Last admission: Cholecystojejunal fistula	Carcinoma of ampulla of Vater: Biopsy, cholecystojejunostomy
G.C. 60-M	Choledochojejunal. History of pancreatoduodenectomy and cholecystectomy for carcinoma of ampullary portion of common bile duct	Epigastric pain, hematemesis, melena	Not recorded	Barium in bile ducts into jejunum. Barium in stomach through gastroenterostomy into jejunum (Fig. 1). Barium in pancreatic ducts (Fig. 2). Later developed marginal ulcer	Had had gastroenterostomy proximal to anastomosis of the pancreas and bile duct with the jejunum. Second operation (for ulcer) revealed active marginal ulcer of gastroenteric stoma which was excised. Jejunojejunostomy, subtotal gastrectomy and vagotomy
C.W. 60-F	Cholecystoduodenal	Right upper quadrant pain and tenderness, vomiting, diarrhea (had a cholecystoduodenostomy for chronic pancreatitis)	Abdominal tenderness	Gastrointestinal study: Barium from gallbladder to duodenum	Cholecystojejunostomy
F.G. 80-F	Postoperative history of carcinoma of common bile duct. Surgery. Choledochoduodenal	Weakness, leg pain (phlebitis)	Pale, thin, liver palpable	Gastrointestinal study: Barium from duodenal bulb to hepatic ducts	Had anastomosis of hepatic duct to duodenum

---

* From the Radiology Department, Misericordia Hospital, Philadelphia, Pennsylvania. Presented in exhibit form at the Annual meeting, Pennsylvania Radiological Society, Pocono Manor, Pennsylvania, May 14, 1960.

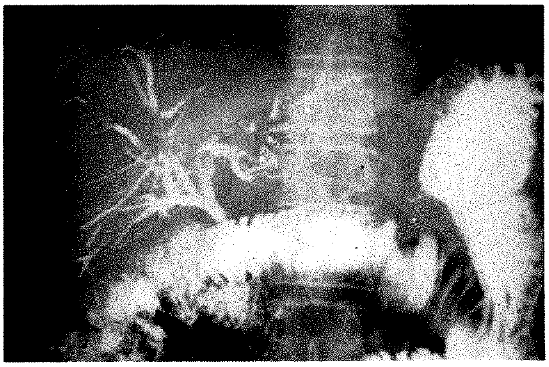


FIG. 1. Barium outlines the biliary tree in a patient following Whipple's operation for carcinoma of the head of the pancreas. Note the gastroenterostomy and loop of small bowel into which the common bile duct has been implanted.

tojejunal, 1; and choledochojejunal, 1. Eleven of our patients were women and 5 were men. The average age was 60 years in the spontaneous cases (range 46–75 years).

From the clinical standpoint biliary fistulae can be classified as spontaneous and postoperative. Postoperative fistulae are most often cholecystoduodenal or cholecystojejunal in type and are formed in the course of treatment of obstructive diseases (stricture or tumor) in the common bile duct area (Table II). Spontaneous biliary fistulae present as one of three clinical syndromes: (1) *cholangitis*, (2) *gastric obstruction*, and (3) *ileus*. Occasionally, a patient will exhibit a clinical picture which is a combination of these three syndromes.

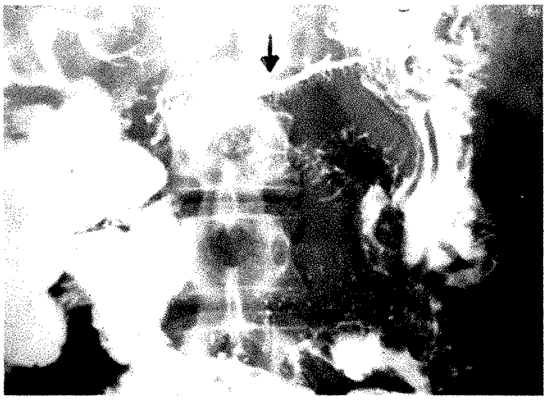


FIG. 2. Same patient as in Figure 1. Barium study shows opacification of the pancreatic duct.

Spontaneous biliary fistulae are usually caused by cholecystitis, generally associated with calculi and chronic in nature, or by duodenal ulcer with perforation into an adjacent adherent gallbladder. Malignant disease and other causes are very rare.

ROENTGENOGRAPHIC FINDINGS

The roentgenographic findings of biliary fistulae are varied. Classically, one may see distended loops of small bowel, air in the biliary tree and a gallstone in an abnormal location. Plain roentgenograms of the abdomen should be made in the supine, erect or decubitus and, sometimes, in the prone position. In cases with obstruction, air-fluid levels are demonstrated in distended loops of small intestine as in any case of intestinal obstruction. If the stomach is obstructed, gastric dilatation will be seen. The reason for the obstruction of these organs may be suspected if one can visualize a "gallstone" in an abnormal position or if a laminated gallstone previously demonstrated but not surgically removed disappears.

Air in the biliary tree may be demonstrated on any of the studies but often is

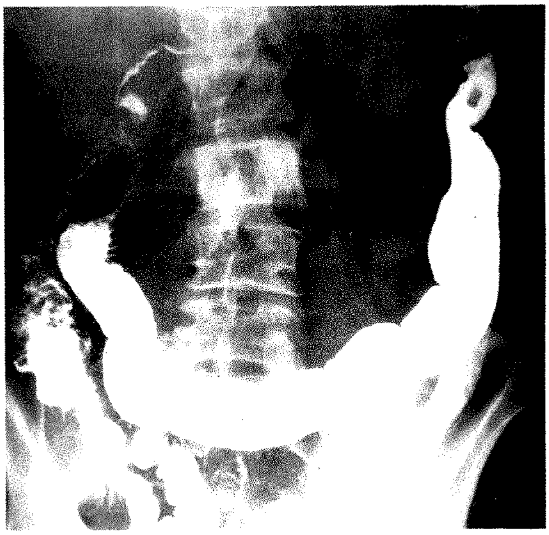


FIG. 3. Case 1. Barium enema study shows cholecystocolic fistula. The gallbladder is contracted and barium also partially outlines the bile ducts.

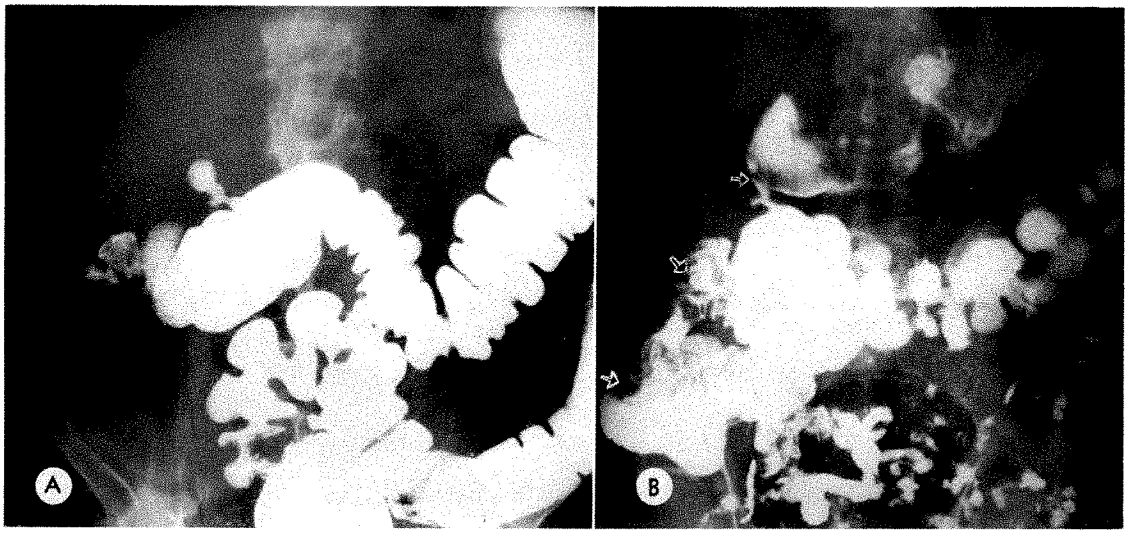


FIG. 4. Case II. (*A*) Barium enema study demonstrates a cholecystocolic fistula distal to the hepatic flexure. There is obstruction to retrograde flow of barium in the hepatic flexure area. (*B*) Three hour roentgenogram of upper gastrointestinal study demonstrates long constricting lesion of ascending colon above the cecum (carcinoma). The cholecystocolic fistula is again seen.

TABLE III

INTERNAL BILIARY TRACT FISTULAE (CHOLANGITIS)

Patient, Age and Sex	Type	Symptoms	Physical Examination	Roentgenographic Findings	Operation
A.McC. 74-F	Cholecystocolic	Right upper quadrant abdominal pain, nausea, vomiting, chills, fever, clay colored stools	Slight abdominal distention, tenderness in right upper quadrant	Scout roentgenogram: Opaque calculus, 1.2 cm. in diameter in right upper quadrant. Air in biliary tree	Calculus cholecystitis. Fistula into hepatic flexure at colon
D.T. 58-F	Cholecystocolic	Right upper quadrant abdominal pain, nausea, vomiting, chills and fever	Tenderness in right upper quadrant and icterus	Barium enema study after first operation: Cholecystocolic fistula (Fig. 3)	First operation: Inflamed biliary tree, gallbladder not identifiable. Second operation: Cholecystectomy and closure of fistula
H.F. 75-M	Cholecystocolic	Right upper quadrant abdominal pain, tarry stools and constipation	Mild tenderness on deep palpation in right lateral abdomen	Cholecystogram: Nonvisualized. Gastrointestinal and barium enema study: Obstructing lesion in ascending colon; fistula from hepatic flexure and colon to gallbladder (Fig. 4, *A* and *B*)	Carcinoma of ascending colon. Cholecystocolonic fistula with calculi in common bile duct and gallbladder. Cholecystectomy and right hemicolectomy
A.D. 62-F	Cholecystoduodenal	Right upper quadrant pain, fatty food intolerance	Right upper quadrant tenderness, rigidity, fever, icterus and ileus	Gastrointestinal study: Large cholecystoduodenal fistula (Fig. 5, *A* and *B*)	None. Large calculus passed per rectum
S.McG. 63-F	Choledochoduodenal	Right upper quadrant pain, fatty food intolerance, nausea, vomiting and icterus	Right upper quadrant tenderness	Cholecystogram: Nonvisualization. Gastrointestinal study: Cholecystoduodenal fistula. Barium in gallbladder and ducts	Cholecystectomy, choledochelithotomy repair at choledochoduodenal fistula
Sr.A. 54-F	Choledochoduodenal	Vomiting, dark urine, history of cholecystectomy, biliary fistula	Abdominal tenderness and jaundice	Gastrointestinal study: Barium in fistula from duodenal bulb to common duct. Choledochoduodenostomy	Re-operation: Stricture at common duct divided and implanted into duodenum

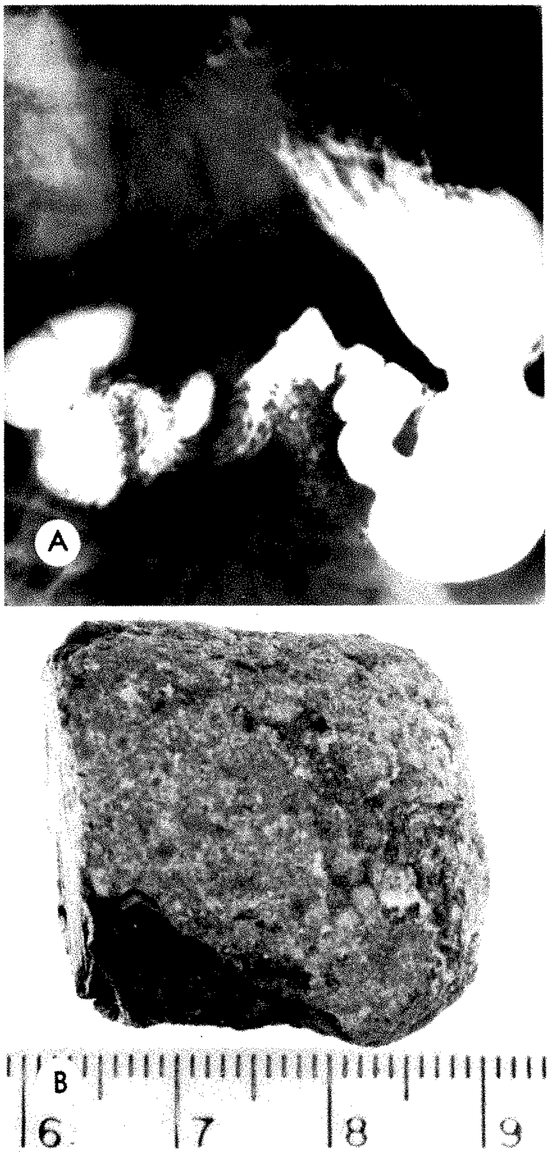


Fig. 5. Case vii. (*A*) Upper gastrointestinal study demonstrates a large cholecystoduodenal fistula in a patient presenting with a cholangitis-like syndrome. (*B*) Large cholelith which passed per rectum several days after onset of symptoms.

best seen on erect roentgenograms made after the patient has been lying on his left side for 5 minutes or has been in the erect position for 5 minutes so as to allow air to rise into the system. The air will have a typical arborized pattern.

For best demonstration of these fistulae barium studies of the upper gastrointestinal tract are performed. The barium enters the biliary tree and outlines all its parts (Fig. 1 and 2). It remains in the biliary system for a variable period of time. We have observed it for as long as 8 days. It has not caused cholangitis in our experience.

ILLUSTRATIVE CASES

(1) *Cholangitis* causes pain in the right upper quadrant of the abdomen, nausea, vomiting, chills, fever and jaundice. It may be acute or intermittent in nature. Cholangitis has occurred in all of our cholecystocolic fistula cases (3) and in 3 of 6 patients with cholecystoduodenal fistulae (Table iii).

Case i. D.T., a 58 year old white woman, was admitted on December 31, 1955 complaining of right upper quadrant pain of 24 hours' duration, nausea, vomiting, chills and fever. Examination revealed an acutely ill, icteric patient with moderate tenderness in the right upper quadrant of the abdomen. The clinical impression was acute cholecystitis. On January 7, 1956, operation revealed an anomalous inflamed biliary tree with many adhesions; a gallbladder was not found at the first operation. The abdomen was closed and the patient recovered satisfactorily. Contrast studies following operation showed a cholecystocolic fistula (Fig. 3). Cholecystectomy and closure of the fistula were carried out and the patient has remained well.

Case ii. H.F., a 75 year old white man, was admitted in August, 1957 complaining of constipation, tarry stools and pain in the right upper quadrant of the abdomen. Single and "double dose" cholecystography showed no gallbladder visualization. Barium enema studies demonstrated an obstructing lesion of the ascending colon and a fistula from the region of the hepatic flexure into the gallbladder (Fig. 4, *A* and *B*). At operation, a carcinoma of the ascending colon was found. There was a cholecystocolic fistula into the proximal portion of the transverse colon. The common bile duct and gallbladder contained stones. A cholecystectomy and a right hemicolectomy were performed. The patient has remained well.

In all 6 of our cases the cholangitis was caused by calculus disease of the biliary

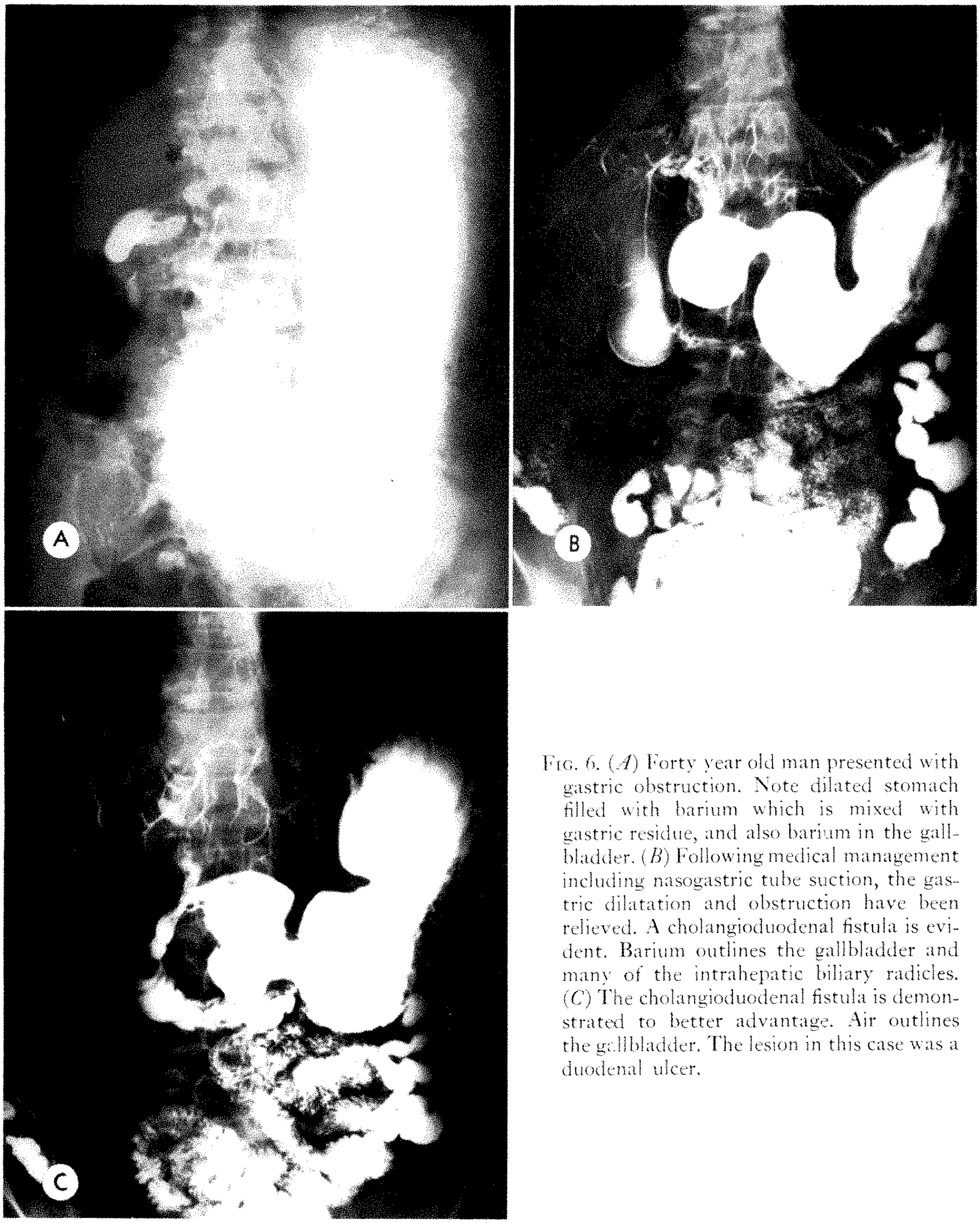


Fig. 6. (*A*) Forty year old man presented with gastric obstruction. Note dilated stomach filled with barium which is mixed with gastric residue, and also barium in the gallbladder. (*B*) Following medical management including nasogastric tube suction, the gastric dilatation and obstruction have been relieved. A cholangioduodenal fistula is evident. Barium outlines the gallbladder and many of the intrahepatic biliary radicles. (*C*) The cholangioduodenal fistula is demonstrated to better advantage. Air outlines the gallbladder. The lesion in this case was a duodenal ulcer.

system. In one very bizarre case, the patient passed a large calculus per rectum (Fig. 5, *A* and *B*).

(2) The patient with *gastric obstruction* and a biliary fistula presents with intractable vomiting and sometimes vague upper abdominal discomfort. A previous history suggestive of biliary tract disease may or may not be obtained. Three of our patients presented with this syndrome (Fig. 6, *A*,

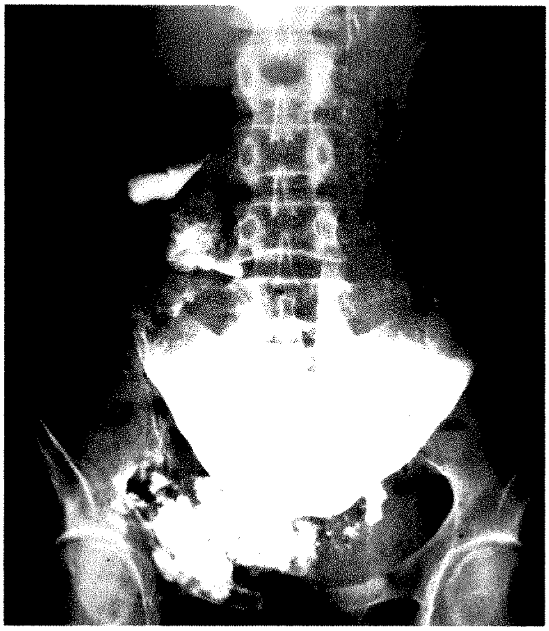


FIG. 7. Case III. Erect roentgenogram of gastrointestinal study showing barium mixed with stomach contents in a dilated obstructed stomach due to duodenal ulcer. A cholecystoduodenal fistula is present. Note air-barium level in gallbladder.

B and *C*). In 2 of them, the fistula was caused by a perforation of a duodenal ulcer and in the third, calculi were found obstructing the duodenum and stomach (Table IV).

CASE III. K.McS., a 43 year old white woman, was seen on November 22, 1955 with a 6 month history of indigestion and vomiting of 3 months' duration. Upper gastrointestinal studies showed the stomach to be obstructed and there was a fistula between the duodenum and gallbladder (Fig. 7). The patient refused surgical treatment. The gastric obstruction was relieved by medical management. Roentgenograms 2 years

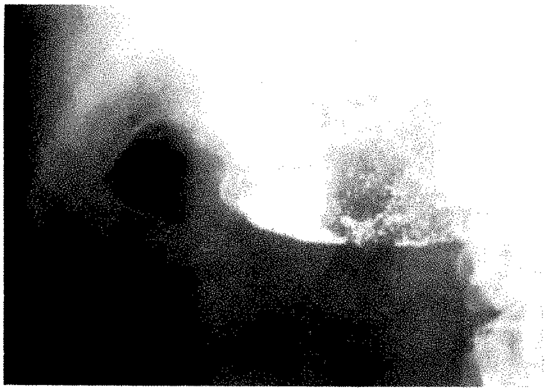


FIG. 8. Case IV. Cholecystogram showing contrast agent in the stomach. A round polyp-like nonopaque lesion is outlined in the gastric antrum.

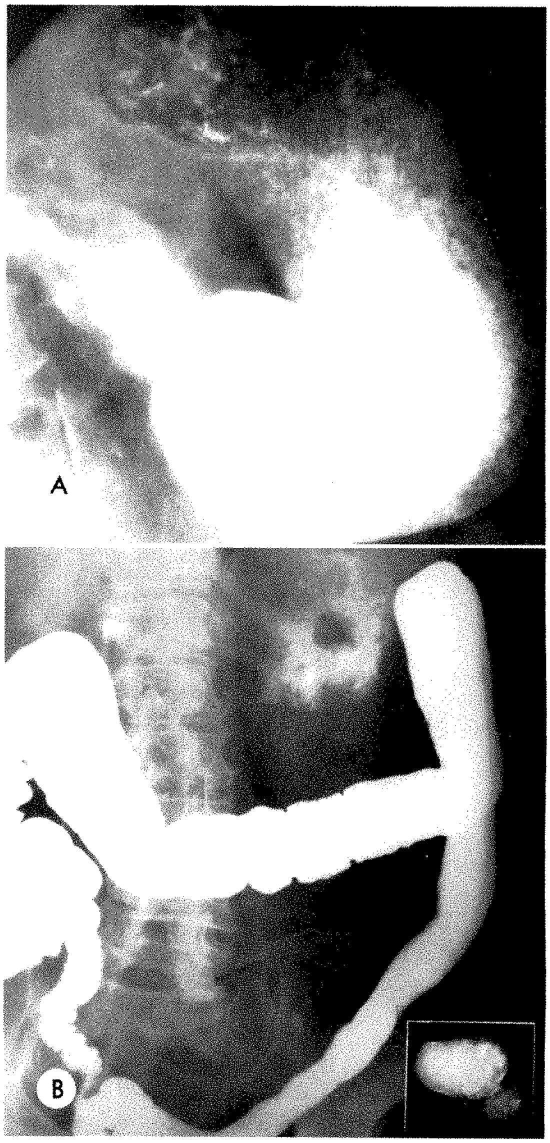


FIG. 9. Case IV. (*A*) Upper gastrointestinal study shows gastric obstruction and a vague "negative" defect in the gastric antrum. (*B*) Barium enema study. Stomach still contains barium outlining the polyp-like defect. Inset shows the roentgenogram of 2 gallstones removed at gastrotomy. Even though these calculi are "opaque" with this technique, they were not seen as opaque bodies on the original "*in vivo*" roentgenograms.

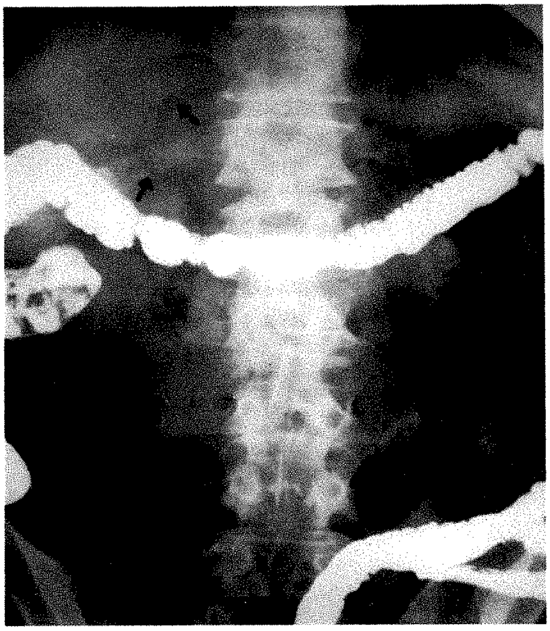


Fig. 10. Case v. Barium enema study demonstrates the classic roentgenographic triad of gallstone ileus—dilated gas filled loops of small intestine, air in biliary tree (arrows) and a laminated calculus in right lower quadrant of abdomen.

later still showed a fistula but she remained symptom-free on an ulcer regimen.

Case iv. J.S., a 66 year old white obese woman, was admitted on September 8, 1955 with a history of vomiting for a period of 10 days and pain in the right upper quadrant. On examination the abdomen was soft with no distention and the peristalsis was slightly hyperactive. Cholecystograms showed contrast medium retained in the stomach (Fig. 8). An upper gastrointestinal series showed gastric obstruction with several large radiolucent defects in the stomach and duodenum (Fig. 9, *A* and *B*). At operation, the duodenum was adherent to the liver and the gallbladder. Several large stones

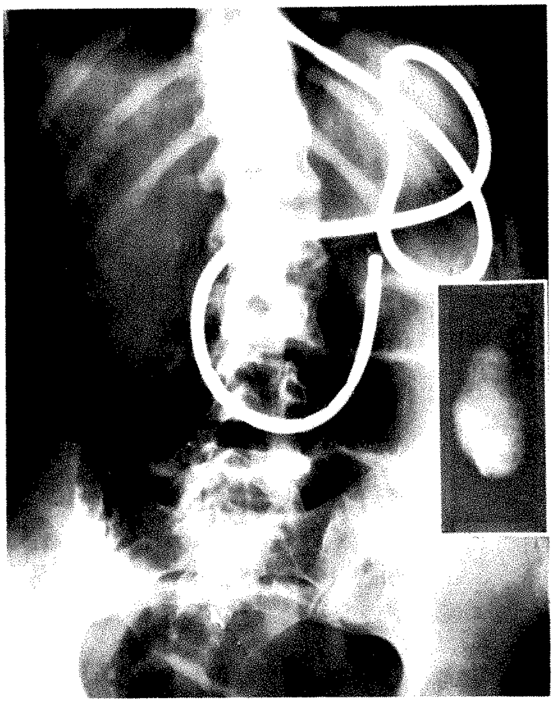


Fig. 11. Case vi. Plain roentgenogram of abdomen shows long intestinal tube in place. Obstructed gas filled loops of small intestine are seen. No opaque calculi are visible. At laparotomy a gallstone was removed from the ileum. Inset shows a roentgenogram of the removed calculus.

Table IV

INTERNAL BILIARY TRACT FISTULAE (GASTRIC OBSTRUCTION)

Patient, Age and Sex	Type	Symptoms	Physical Examination	Roentgenographic Findings	Operation
J.T. 40-M	Cholangioduodenal	Nausea, vomiting, belching and distention, history of duodenal ulcer and duodenal diverticulum; had diverticolectomy	Epigastric distention	Gastrointestinal study: Large cholangioduodenal fistula, air and barium in biliary tree, stomach obstructed (Fig. 6, *A*, *B* and *C*)	None. Gastric section, parenteral fluids, vitamins and ulcer diet
K.McS. 43-F	Cholecystoduodenal	Indigestion, nausea and vomiting for 3 months	Slight distention	Gastrointestinal study: Stomach obstructed, fistula of duodenum and gallbladder (Fig. 7)	Refused
J.S. 66-F	Cholecystoduodenal	Right upper quadrant abdominal pain and vomiting	Slightly hyperactive peristalsis	Cholecystogram: Retained in stomach (Fig. 8). Gastrointestinal study: Obstruction with several large filling defects in stomach and duodenum (Fig. 9, *A* and *B*)	Duodenum adherent to liver and gallbladder. Several large stones removed from stomach and duodenum

TABLE V

INTERNAL BILIARY TRACT FISTULAE (ILEUS)

Patient, Age and Sex	Type	Symptoms	Physical Examination	Roentgenographic Findings	Operation
J.H. 70-M	Choledochoduodenal	Right upper quadrant pain, nausea and vomiting	Slight icterus, normal peristalsis, no tenderness	Scout roentgenogram: Gallstone in right lower quadrant, small bowel distention and air in biliary tree. Barium enema study. Colon normal (Fig. 10)	Gallstone in distal ileum, distended small bowel
M.T. 46-F	Cholecystoduodenal	Intermittent vomiting for 5 weeks, periumbilical pain, and constipation	Abdomen firm and tympanitic, hypoactive bowel sounds	Scout roentgenogram: Dilated small bowel (Fig. 11)	Bowel distended. Large gallbladder calculus removed from terminal ileum, enterostomy
M.O'D. F	Cholecystoduodenal	Vomiting and abdominal pain	Mildly distended abdomen. hypoactive peristalsis	Patient unable to take barium, even vomited when barium passed through Levine tube into stomach. Scout roentgenogram: Distended small bowel loops. Air in biliary tree	Laparotomy: Gallstone obstruction at terminal ileum, adhesions in region of gallbladder

were removed from the stomach and duodenum. The patient had an uneventful postoperative course and has remained well.

(3) *Ileus* due to gallstone obturation often presents with the classic symptoms of intestinal obstruction: colicky abdominal pain, distention, absence of bowel movements and vomiting. The patient is more often a woman and may be of any age. In older persons, the classic symptoms may be absent and vomiting without pain or distention may be the predominant symptom. The gallstone may not contain enough calcium to be roentgenographically visible (Case VI) and the diagnosis may not be made prior to operation. Our series includes 3 cases (Table V).

CASE V. J.H., a 70 year old white man, was admitted on August 10, 1954 complaining of pain in the right upper abdomen, nausea and vomiting. Examination revealed slight icterus, normal peristalsis and no abdominal tenderness. Scout roentgenogram of the abdomen and barium enema study showed a gallstone in the right lower quadrant of the abdomen, gas filled loops of the small bowel and air in the biliary tree. The colon was normal (Fig. 10). At operation, the small bowel was dilated and the gallstone was removed from the distal ileum. Three days postoperatively he expired as a result of coronary occlusion.

CASE VI. M.T., a 46 year old white woman, was admitted on February 19, 1957 with intermittent vomiting for a period of 5 weeks, periumbilical pain and constipation. The abdomen was firm and tympanitic with hypoactive bowel sounds. Roentgenograms of the abdomen showed loops of dilated, fluid-filled small bowel. No calculi were seen and there was no air in the biliary tree (Fig. 11). At laparotomy, the bowel was found to be distended and a large gallstone was removed from the terminal ileum. A roentgenogram of the calculus showed little calcium. Her wound dehisced several days after secondary wound closure. The patient began to have melena and hematemesis and expired. Autopsy permission was not granted.

In some cases *cholangitis and ileus* may both be present as illustrated by Case VII.

CASE VII. A.D., a 62 year old white woman who had a long history of fatty food intolerance, was admitted in November, 1949 with right upper quadrant pain, tenderness, rigidity and fever. Ileus developed and 2 days after admission she passed a large stone from her rectum (Fig. 5*B*). Following this she rapidly improved. Upper gastrointestinal study showed a large cholecystoduodenal fistula (Fig. 5*A*).

SUMMARY

Sixteen cases of biliary fistulae demonstrated roentgenographically are discussed. The clinical features of spontaneous biliary fistula—cholangitis, gastric obstruction and ileus—are described. The classic roentgenographic findings of small bowel distention, air in the biliary tree, abnormally

located calculus and the contrast medium visualization of fistula are illustrated.

C. Jules Rominger, M.D.
Department of Radiology
Misericordia Hospital
54th Street and Cedar Avenue
Philadelphia 43, Pennsylvania

The authors are grateful to the following for permission to include their patients in this report: Dr. Richard Flandreau, Dr. Eugene Garvin, Dr. Donald Geist, Dr. John Keveney, the late Dr. Francesco Mogavero, Dr. David McAleer, Dr. Francis McGinnis and Dr. William Zintl.

REFERENCES

1. Arango, O., and Marmolejo, A. Fistula biliares internas. *Acta radiol. Interamericana*, 1955, *5*, 43–62.
2. Longley, N. B., and Margulis, A. R. Roentgenographic findings in cases of gastric biliary calculi. *Surgery*, 1961, *49*, 719–722.
3. Shehadi, W. H. Roentgenologic observations in cases of fistulae of biliary tract. *J.A.M.A.*, 1960, *174*, 2204–2208.
4. Shehadi, W. H. Clinical Radiology of the Biliary Tract. McGraw-Hill Book Company, Inc., New York, 1963, pp. 249–260.

A STUDY OF FIXED FILLING DEFECTS IN THE WELL OPACIFIED GALLBLADDER AND THEIR EVOLUTION

By R. VINCENT GRIECO, M.D.,* NOEL F. BARTONE, M.D.,* *and* ANTHONY VASILAS, M.D.†
NEW YORK, NEW YORK

ROENTGENOGRAPHICALLY demonstrated small, fixed filling defects in a well opacified gallbladder are frequently referred to as papillomas or polyps. Despite the fact that these lesions have been shown repeatedly, with rare exceptions, to be nonmalignant,[5,17] it is still commonly felt that premalignancy must be seriously considered. This point of view in part is a carry over of impressions obtained from studies of small polypoid masses found in the colon, of which a significant number is malignant.[11,12,16] Obviously, patients with small fixed gallbladder lesions who undergo cholecystectomy shortly after the cholecystographic examination cannot be evaluated satisfactorily for potentialities of malignancy.[4] If, however, a number of these patients could be kept under observation for a significant period of time without hazard, and then, as clinical evidence warrants, the gallbladder were removed, it follows that a more realistic impression of the evolution of these filling defects could be obtained. This report deals with such an approach.

MATERIALS AND METHODS

We have studied 50 cases with the gallbladder showing excellent concentration of contrast material in which a single or several small fixed radiolucent defects were present. These cases are analyzed in detail in Tables I through VIII. Twenty four patients were operated upon for removal of the gallbladder (Table II), 14 within 6 months after cholecystographic diagnosis; the other 10 had cholecystectomy 6 months to 6 years after the original roentgen diagnosis and each of these had a re-check cholecystographic examination shortly before surgery.

Table I

PATIENTS WITH RADIOLUCENT DEFECTS IN THE WELL CONCENTRATED GALLBLADDER

	Operated	Non-operated	Total
No. of Patients	24	26	50
Males	2	6	8
Females	22	20	42
Age (yr.)			
20–30	4	2	6
31–40	2	4	6
41–50	4	7	11
51–60	6	10	16
61+	4	7	11

Table II

DURATION OF FOLLOW-UP STUDIES BY CHOLECYSTOGRAPHY

	Operated	Non-operated	Total
0–6 months	14	19	33
6 months–1 year	1	1	2
1–2 years	3	1	4
3–4 years	1	1	2
4–5 years	3	3	6
5–6 years	2	0	2
7–8 years	0	1	1

Of the 26 nonoperated cases, 7 had follow-up roentgen studies of the gallbladder from 6 months to 8 years after the initial roentgenologic diagnosis. Eight cases had clinical follow-up only and these were all asymptomatic with reference to the gallbladder. The remaining 11 cases had neither roentgenographic nor clinical follow-up studies.

---

* Attending Radiologist, Methodist Hospital, Brooklyn, New York.
† Attending Radiologist, Beekman-Downtown Hospital, New York, New York.

Figure 1 shows the locations of the fixed radiolucent zones of our cases.

ROENTGEN ANALYSIS OF OUR MATERIAL

There is little to be added to Kirklin's[8,9] description of the cholecystographic appearance of these lesions, which may be summarized as consisting of one or more small round or oval, fixed, radiolucent defects in a well concentrated gallbladder which are often better delineated in the contracted viscus. Such roentgen findings may represent several different pathologic entities, [1,20,22] *i.e.*, adenomas, adenomyomas, cholesterol polyps and fixed stone (Table v and Fig. 2, *A–D*). A number of our cases showed other associated roentgen findings such as mobile stones, Rokitansky pouches, a short stalk and the presence of stippled texture of the fixed lesion (Table iv). It is unfortunate that except for adenomyomas there are no distinguishing roentgen features which can differentiate the various lesions.[6] Adenomyoma, of which there were 7 in this series, characteristically are found at or near the fundus, are usually larger than other lesions and may appear umbilicated.

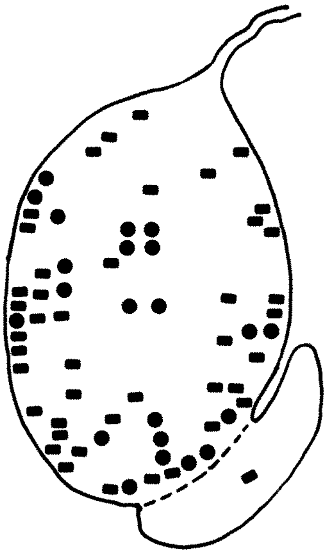


Fig. 1. Sketch showing the locations of the fixed radiolucent defects in our cases. ● = operated cases; ■ = nonoperated cases.

Table III

FIXED LESIONS PER CASE SHOWN ROENTGENOGRAPHICALLY

No. of Lesions per Case	Operated	Non-operated	Total No. of Patients	Total No. of Lesions
1	11	22	33	33
2	4	8	12	24
3	1	2	3	9
4	1	0	1	4
5	1	0	1	5
			50	75

Table IV

ASSOCIATED ROENTGEN FINDINGS

	No. of Cases		
	Operated	Non-operated	Total
Gallstones	3	4	7
Aschoff-Rokitansky sinuses	2	1	3
Stalk*	2	4	6
Punctate dimpling or stippling†	7	15	22

* When the stalk was visible roentgenographically, it was very short.

† By dimpling or stippling is meant pin point areas of increased density within the radiolucent defect seen within the well opacified gallbladder, suggesting an irregular cryptic surface to the fixed lesion.

Three of our cases of adenomyoma have had follow-up studies at 14 months, 2 years, and 5 years, respectively, without any change in roentgen appearance (Fig. 3, *A* and *B*). Ochsner[13] has described the differing configurations of adenomyomas depending upon various phases of contraction of the gallbladder.

Of those cases which had a follow-up study (Table vi), most of the lesions showed no significant change in size, shape, position or number. There was no appreciable change in the concentrating ability of the gallbladder (Fig. 4, *A* and *B*). On follow-up roentgen studies, Eelkema *et al.*[3] reported a decrease in concentrating power in a few cases but none of our cases showed any decrease in concentrating ability. In

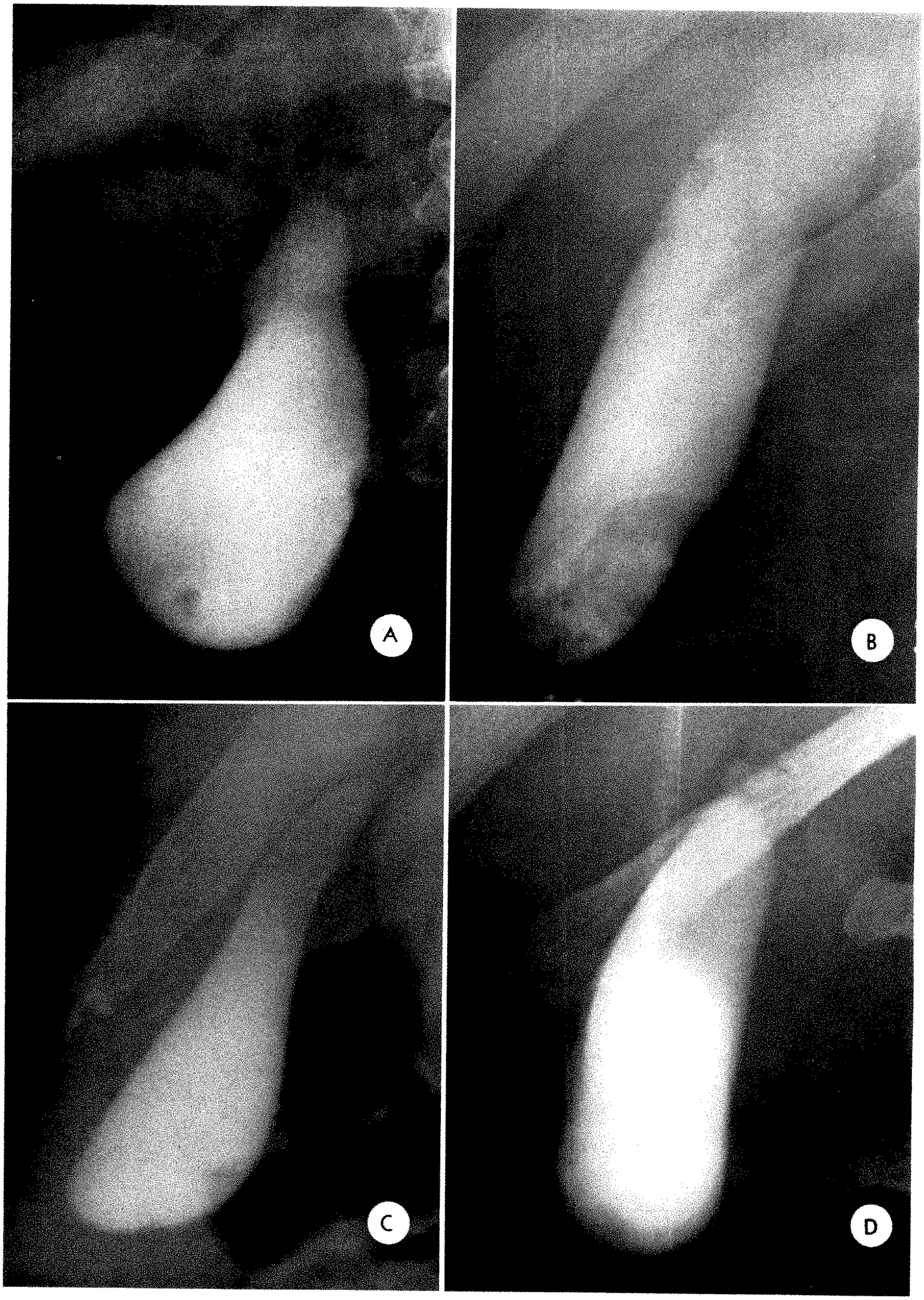


FIG. 2. Examples of different pathologic entities producing similar roentgen findings. (*A*) Fixed stone. (*B*) Two adenomas. (*C*) Cholesterol polyp. (*D*) Adenomyoma.

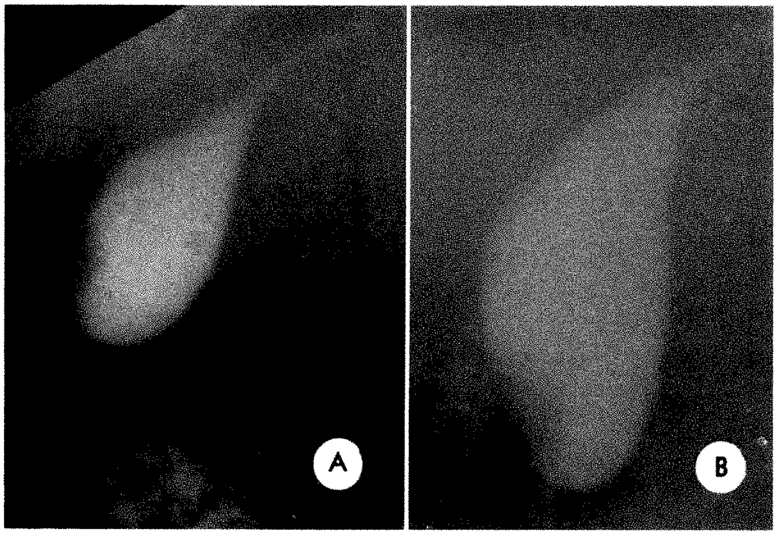


FIG. 3. CASE JC. Disappearance of a radiolucent defect. (*A*) Initial study in 1959 shows adenomyoma near fundus and a round radiolucent filling defect in the body. (*B*) Two years later there is no change in the adenomyoma; the small round filling defect noted on the original study is not observed on this study. Adenomyoma only was found at surgery.

some patients, slight increase in the size of the radiolucency was observed (Fig. 5, *A* and *B*; and 6, *A*, *B* and *C*). Occasionally, there may be an increase in the number of visualized lesions; this presumably indicates either the formation of new lesions, fixed and/or mobile, during the period of observation, or a sufficient increase in size so that the lesion previously not visible can now be seen.

Finally, the radiolucent defect may become invisible on a subsequent cholecystogram (Fig. 3*B*). Our group included 2 such cases and other workers have reported sim-

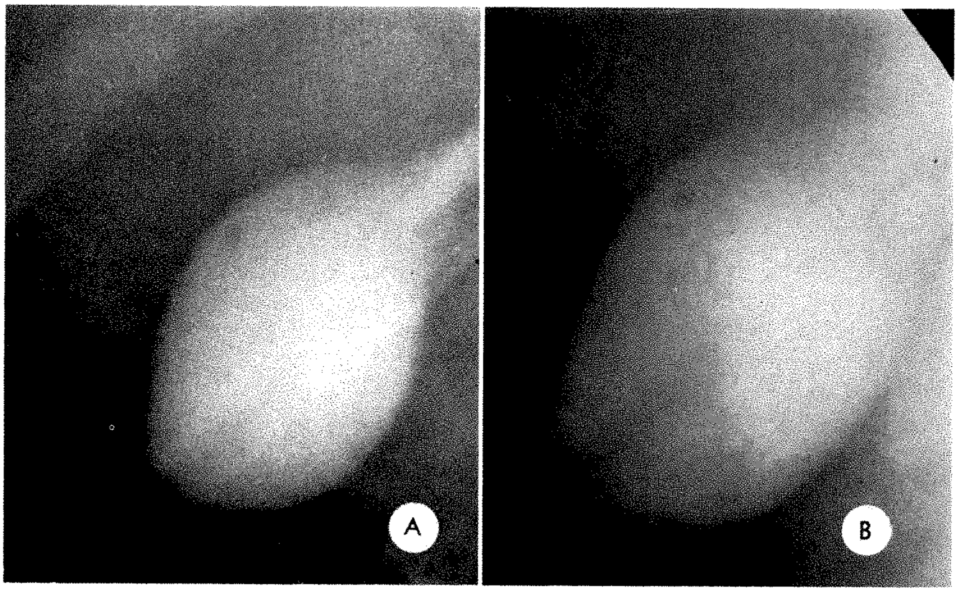


FIG. 4. CASE ER. No change in fixed filling defect. (*A*) Initial study in 1957 shows a fixed radiolucent defect. (*B*) Four years later there is no change in the size of the fixed lesion or in the concentrating ability of the gallbladder. Two additional years of clinical follow-up revealed no gallbladder symptomatology.

TABLE V

PATHOLOGIC DIAGNOSIS IN THE 24 OPERATED CASES WITH REFERENCE TO THE FIXED LESIONS ON THE CHOLECYSTOGRAM

Pathologic Diagnosis	No. of Cases
Adenomyoma	7
Adenomatous polyps	2
Focal cholesterolosis*	10
Stone fixed to the wall of gallbladder	2
Single or multiple mobile stones; no polyps or cholesterolosis	2
Nothing reported at surgical pathologic examination	1
Additional pathologic findings besides presence or absence of mobile stones	
General chronic cholecystitis	8
Focal cholecystitis	2

* The pathologist at times qualified this diagnosis at his discretion depending on the size of the lesion as to presence or absence of a polypoid mass or papilloma.

ilar findings.[3] One may speculate as to the possible reasons for the disappearance of a fixed lesion on subsequent examinations as one or more of the following: (1) Dense opacification obscuring the defect; (2) breaking off of the lesion and then passing through the cystic duct or remaining to become a nidus for a mobile stone; (3) actual resolution of the patholgic process; (4) inadequate roentgen technique and/or misdiagnosis on the initial or later roentgen examination; and (5) poor opacification offering insufficient contrast.

DISCUSSION

Exclusive of adenomyomas and stones, the overwhelming number of operated cases, both ours (Table v) and those of others,[10,17,22] are associated in some form or other with cholesterol deposits. These cholesterol polyps may be considered as one group in which the malignant propensities *per se* are nil.

Adenomyomas or myoepithelial anomalies are probably not clinically significant and usually are considered malformations,[6,13] although it must be realized that the distinction among malformations, hyperplasia and new growth is frequently blurred and difficult to define.

Our experience and the experience of others[7,19,20,23] clearly indicate that there are

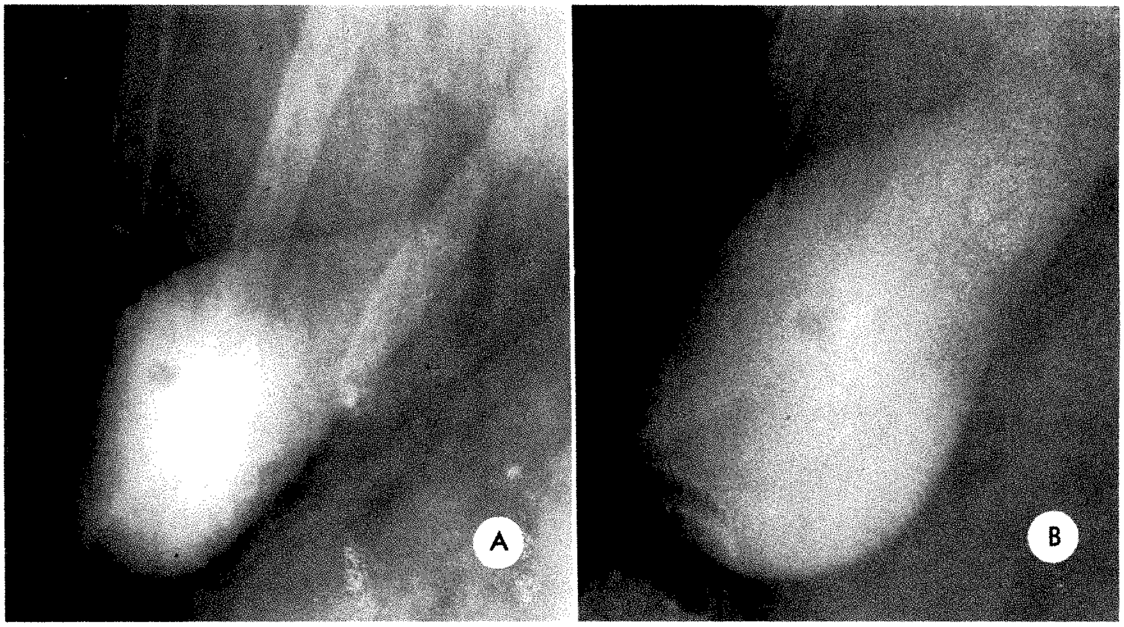


FIG. 5. CASE IR. Slight increase in size. (*A*) Initial study in 1954. (*B*) Six years later there is slight change in the size of the fixed defect but there is no loss of concentrating ability. Surgery revealed cholesterol polyp.

relatively few cases of small, fixed lesions in a well concentrating gallbladder which might represent true tumors and practically all are unquestionably benign. Such cases can be kept under excellent observation for months and years by periodic chloecystography. In our series, the pathologic findings indicate only 2 cases of true tumor formation and both proved to be benign. Unfortunately, these 2 cases had no roentgen follow-up study prior to surgery.

During the period of observation, the conservative "wait and see" attitude in the nonoperated group and in the delayed operated group shows nothing clinically or roentgenographically which can be interpreted as having been harmful to the patient, except possibly in 2 cases where there was formation of stones in the interim.

Although we had no case showing more than a 3 mm. increase in size of the lesion in the follow-up study, it would be reasonable to assume that any greater increase in size, even in an asymptomatic patient, would call for surgical intervention on the grounds that in theory it might represent a suspect lesion. It is to be noted that except for adenomyomas, the overwhelming majority of the lesions we have been discussing are under 5 mm. in size (Table VII). The question may be asked: "Do lesions of 1 cm. or more in size have a different potential as far as malignancy is concerned?"

Table VI

INCREASE IN SIZE OF THE FIXED LESIONS IN MM. DURING FOLLOW-UP PERIOD OF MORE THAN 6 MONTHS

Increase in Size	No. of Cases		
	Operated	Nonoperated	Total
None	4	6	10
1–2 mm.	3	1	4
2–3 mm.	1	0	1

Two other cases originally described as fixed lesions were found to increase in size and become mobile stones.

An apparent slight increase in size is open to question (see Fig. 6, *A–C*).

Table VII

SIZE OF EACH FIXED LESION IN MM. ON THE ORIGINAL CHOLECYSTOGRAM

Size	Operated	Nonoperated	Total
3 mm. or less	19	22	41
3–4 mm.	4	10	14
4–5 mm.	4	4	8
5–6 mm.	1	2	3
6–7 mm.	2	1	3
10 mm.*	2	3	5
15 mm.†	0	1	1
Total fixed lesions			75

* These lesions on operation proved to be adenomyomas; nonoperated case had roentgen appearance suggesting adenomyoma.

† The roentgen appearance suggested a cluster of small lesions rather than a single large lesion.

Since it is axiomatic that a single lesion, if malignant, is malignant from its inception, the small size of a lesion cannot, *per se*, be used as a criterion as to its benign, or malignant nature. This is true roentgenographically and frequently on gross pathologic study. Roentgenographically, however, with increase in size of a single lesion, other associated characteristics may appear, such as alteration of contour or surrounding architecture, or dysfunction of the part or organ in question. These collateral findings facilitate the evaluation of malignant possibilities of the observed lesion. Therefore, the question of size is pertinent in relation to malignant potentialities only because of the presence of other characteristics of the lesion, such as contours, density, associated changes in the adjacent architecture or even findings at a distance, which are more readily discernible than when the lesion was only a minute focus, albeit malignant. Furthermore, the increase in size of the primary malignant lesion is not directly related to its other potentialities such as the rapidity and extension of metastases or invasion so that the "silent" metastasis or invasion may become extensive while the visible primary lesion is still small. Or else the metastatic lesions may become roentgenographically visible even though the primary lesion is small and "silent." While there is hardly any doubt that such small

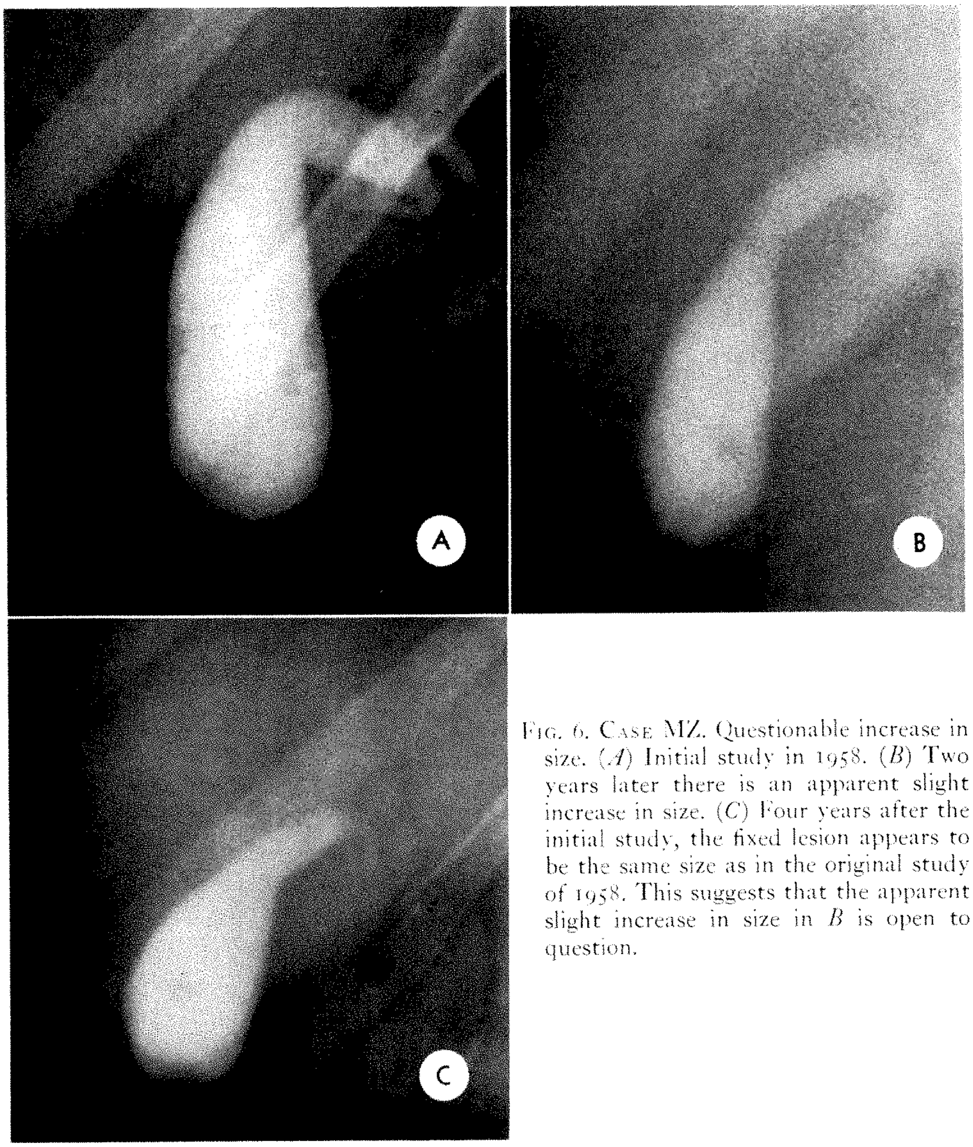


FIG. 6. CASE MZ. Questionable increase in size. (*A*) Initial study in 1958. (*B*) Two years later there is an apparent slight increase in size. (*C*) Four years after the initial study, the fixed lesion appears to be the same size as in the original study of 1958. This suggests that the apparent slight increase in size in *B* is open to question.

lesions in a well concentrating gallbladder are not malignant, if one is confronted with a lesion of 1 cm. or more in size, one must consider whether or not such a larger lesion has a greater probability of being malignant. In practice, however, except for the fundic adenomyomas such larger lesions have rarely been seen. Also, is the yardstick of 7 or 8 years sufficient for evaluating the biologic evolution of these fixed radiolucent lesions? The Mayo group[8] have follow-up studies on many of their cases for 15 years without evidence of carcinoma developing in the gallbladder in which fixed small lesions were present.

Only rare cases have been reported with roentgen evidence of a filling defect in a visualized gallbladder which on pathologic study were discovered to be noninvasive carcinoma or carcinoma *in situ*.*[2,14,15,21] Detection of a carcinomatous gallbladder lesion by cholecystography is extremely

---

* Personal Communication: Dr. Ochsner reports that his 2 cases which were followed-up for 4 years post surgery have remained well; Dr. Cimmino reports that his was lost to follow-up several months after surgery; and Dr. McNeer reports that none of his reported cases had died of cancer.

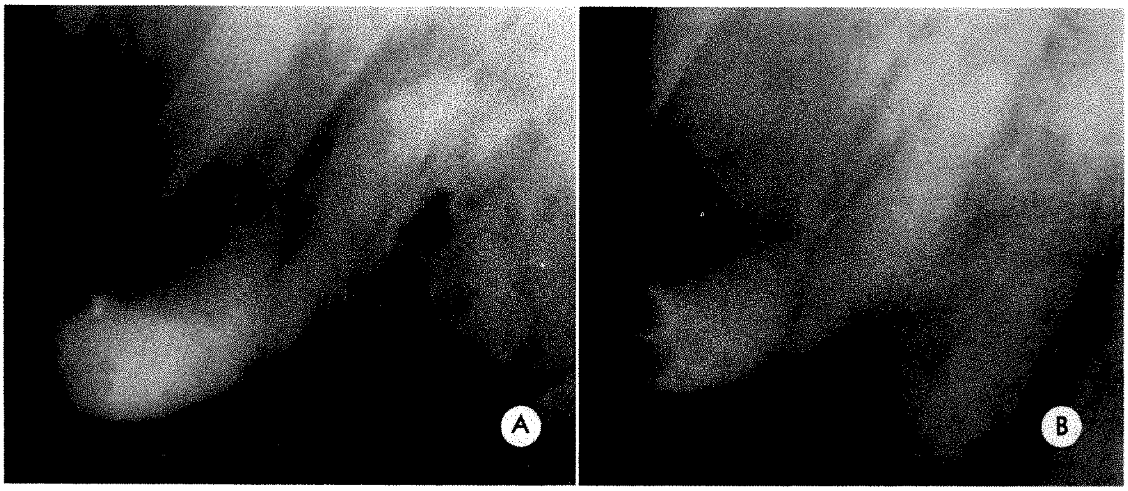


Fig. 7. Case TD. Change from fixed defects to mobile calculi. (*A*) Initial study in 1958 shows 2 small fixed defects. (*B*) Two years later there is disappearance of the fixed defects and appearance of mobile defects (calculi).

rare because such gallbladders demonstrate very poor or no concentration of the opaque medium. This is so, even when malignant involvement is not extensive and there is no obstruction of the biliary tree.

Loss of concentrating function is apparently related to changes in the wall caused by chronic infection which is invariably present in cholecystic carcinoma with or without stones. For practical purposes, therefore, invasive carcinoma of the gallbladder can be excluded in any gallbladder that is well visualized cholecystographically with one routine dose of contrast material. It seems possible that with wider use of the newer contrast media now available, both intravenous and oral, opacification of the gallbladder may occur even with loss of its concentrating ability. These newer media are already sufficiently concentrated by the time they pass through the liver and bile ducts so that there often is visualization of the major biliary radicles. It is not unreasonable to hope that if this concentrated material can enter the carcinomatous gallbladder it may be possible to visualize filling defects and other changes brought about by malignant disease and thus make earlier diagnosis possible.

A study of the 47 cases of carcinoma of the gallbladder at the Methodist Hospital was carried out by Sawyer and Minnis[18] up to 1953 and has been continued by us to date covering a period of 25 years. Twenty four cases had cholecystography; 20 showed nonvisualization, and 3 showed poor visualization, 2 of which contained multiple calculi. Only one case of carcinoma of the gallbladder was found in which there was visualization of the contrast material within the gallbladder. In this case there was very poor visualization after the first dose; however, on repeat dose within 24 hours, visualization was good and multiple calculi were demonstrated. No fixed defect was discernible. Surgical examination revealed only chronic cholecystitis with stones but on careful pathologic study a minute focus (less than 1 mm. in size) of adenocarcinoma was observed near the fundus, which had invaded the wall of the gallbladder and had extended into the serosa. At the time of the surgery, no other objective findings in the liver, lymph nodes or adjacent organs were apparent. This patient expired 4 years post surgery from a hypertensive cerebrovascular accident. At postmortem study, a routine section through one of the lumbar vertebrae revealed an island of adenocarcinoma approximately 1 cm. in size, identical in type to the original lesion found 4 years previously

Table VIII

DEGREE OF GALLBLADDER SYMPTOMATOLOGY

Degree of Symptomatology	No. of Cases		
	Operated	Nonoperated	Total
0–1+	2	15	17
++	8	9	17
+++	6	1	7
++++	8	1	9

in the gallbladder. The organs about the biliary bed including the liver, pancreas and duodenum were free of carcinoma at the time of the postmortem examination.

CONCLUSIONS

1. The well concentrating gallbladder containing one or more small, fixed filling defects is in the overwhelming majority of cases associated with some form of cholesterol deposits. They are not related to malignant changes.
2. Tumors, roentgenographically manifested as a small fixed radiolucent zone in a well visualized gallbladder, are almost always benign.
3. Only the exceptional lesion which shows obvious increase in size, even if asymptomatic, could be considered suitable for surgery on the grounds that in theory it might be suspect.
4. Symptomatic lesions may be suitable for surgery, but only because of the symptoms they produce and not because of any malignant potentiality (Table VIII).
5. Up to the present time, the carcinomatous gallbladder very rarely concentrates sufficient material to demonstrate the lesion, and, with extremely few exceptions, malignancy can be excluded in any gallbladder where the concentrating ability is unimpaired as demonstrated by routine cholecystography.
6. The contention that the small, immobile, mural radiolucent area in the well opacified gallbladder is potentially malignant can be disregarded. A conservative approach is indicated and if the symptoms are mild, the patient may be kept under observation clinically and by cholecystography for years.

SUMMARY

The small, fixed defect in the roentgenographically well concentrated gallbladder, is, with very rare exceptions, benign. If the clinical symptoms are mild, surgery is not indicated and the patient may be followed for years. This conservative attitude is supported by a study of 50 cases. A perusal of the literature strengthens this conservative point of view.

Anthony Vasilas, M.D.
Beekman-Downtown Hospital
170 William Street
New York 38, New York

REFERENCES

1. Carrera, G. M., and Ochsner, S. F. Polypoid mucosal lesions of gall bladder. *J.A.M.A.*, 1958, *166*, 888–892.
2. Cimmino, C. V. Carcinoma in well-functioning gallbladder. *Radiology*, 1958, *71*, 563–564.
3. Eelkema, H. H., Hodgson, J. R., and Stauffer, M. H. Fifteen year follow-up of polypoid lesion of gallbladder diagnosed by cholecystography. *Gastroenterology*, 1962, *42*, 144–147.
4. Grego, J. G., and Harkins, H. N. Polyposis of gall bladder: report of case diagnosed preoperatively by roentgenologic examination. *Am. J. Surg.*, 1944, *63*, 398–401.
5. Illingworth, C. F. W. Carcinoma of gallbladder. *Brit. J. Surg.*, 1935, *23*, 4–18.
6. Jones, H. W., and Walker, J. H. Correlation of pathologic and radiographic findings in tumors and pseudotumors of gallbladder. *Surg., Gynec. & Obst.*, 1957, *105*, 599–609.
7. Kane, C. F., Brown, C. H., and Hoerr, S. O. Papilloma of gall bladder. *Am. J. Surg.*, 1952, *83*, 161–164.
8. Kirklin, B. R. Cholecystographic diagnosis of papillomas of gall bladder. Am. J. Roentgenol. & Rad. Therapy, 1931, *25*, 46–50.
9. Kirklin, B. R. Cholecystographic diagnosis of neoplasms of gall bladder. Am. J. Roentgenol. & Rad. Therapy, 1933, *29*, 8–16.
10. Loitman, B. S., Cassel, M. A., and Holtz, S. Papillomas of gall bladder. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *88*, 783–791.
11. Mackie, J. A., Miller, L. D., and Fitts, W. T. Polyps and polypoid lesions of large bowel "Surgical considerations." *S. Clin. North America*, 1962, *42*, 1451–1465.
12. Nugent, F. W., Meissner, W. A., and Hoel-

SCHER, F. E. Significance of gall bladder polyps. *J.A.M.A.*, 1961, *178*, 426–428.

13. OCHSNER, S. F. Adenomyoma of gall bladder. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1962, *88*, 778–782.
14. OCHSNER, S., and GAGE, M. Papilloma of gallbladder with carcinoma in-situ. *Ochsner Clin. Rep.*, 1956, *2*, 27–31.
15. OCHSNER, S. F, and OCHSNER, A. Benign neoplasms of gallbladder. *Ann. Surg.*, 1960, *151*, 630–637.
16. ORTMAYER, M. Carcinoma in small polyps of distal colon: sigmoidoscopic and histologic study. *Gastroenterology*, 1956, *31*, 404–413.
17. PHILLIPS, J. R. Papilloma of gall bladder. *Am. J. Surg.*, 1933, *21*, 38–42.
18. SAWYER, C. D., and MINNIS, J. F., JR. Primary carcinoma of gall bladder. *Am. J. Surg.*, 1956, *91*, 99–105.
19. SELZER, D. W., DOCKERTY, M. B., STAUFFER, M. H., and PRIESTLEY, J. T. Significance of gall bladder papillomas. *Am. J. Surg.*, 1962, *103*, 472–476.
20. SHEPARD, V. D., WALTERS, W., and DOCKERTY, M. B. Benign neoplasms of gall bladder. *A.M.A. Arch. Surg.*, 1942, *45*, 1–18.
21. TABAH, E. J., and MCNEER, G. Papilloma of gall bladder with in situ carcinoma. *Surgery*, 1953, *34*, 57–71.
22. TEN EYCK, E. A. Fixed defects in gall bladder wall. *Radiology*, 1958, *71*, 840–846.
23. WELLBROCK, W. L. Occurrence and possible significance of adenoma of gall bladder. *Am. J. Surg.*, 1934, *24*, 358–360.

* * *

CLINICAL EVALUATION OF A NEW INTRAVENOUS CHOLANGIOGRAPHIC MEDIUM: 5,5′-SEBACOYL-DIIMINO-BIS (2,4,6-TRIIODO-N-METHYLISOPHTHALAMIC ACID)*

A PRELIMINARY REPORT

By THOMAS R. MARSHALL, M.D., *and* J. T. LING, M.D.
LOUISVILLE, KENTUCKY

THIS is a preliminary report on our clinical experience with a new contrast medium for use in intravenous cholangiography. This new substance was made available to us, under the code designation MP-271,* as the sterile aqueous 75 per cent w/v N-methylglucamine salt solution of 5,5′-sebacoyl-diimino-bis (2,4,6-triiodo-N-methylisophthalamic acid). This acid has a molecular weight of 1,310 and an iodine content of 58.16 per cent. The chemical structure is shown in Figure 1. MP-271 contains 33.6 per cent organically bound iodine and 6.72 gm. of iodine per 20 cc. dose. This represents a higher iodine content than that of the only other currently available intravenous cholangiographic medium, iodipamide methylglucamine (Table I).

Pharmacologic studies conducted by the manufacturer indicate a low order of toxicity for MP-271.[3] The acute intravenous LD_{50} in mice is 13,100 mg./kg. For comparative purposes, an intravenous LD_{50} carried out on iodipamide methylglucamine was determined to be 4,120 mg./kg., approximately one-third that of MP-271. Additional acute toxicity studies conducted on albino rats and mongrel dogs with intravenously administered MP-271 resulted in values of 6,600 mg./kg. and greater than 10,000 mg./kg., respectively. The acute intracerebral LD_{50} of MP-271 in mice is estimated to be 1,120 mg./kg. and for iodipamide methylglucamine it is 62.1 mg./kg. These toxicity studies are presented in outline form in Table II.

TABLE I

COMPARATIVE PHYSICAL PROPERTIES

Product	Salt Concentration (per cent)	Iodine Content (per cent)	Gm. I_2 per 20 ml. dose
MP-271	75	33.6	6.72
Iodipamide Methylglucamine (cholografin methylglucamine)	52	26	5.2

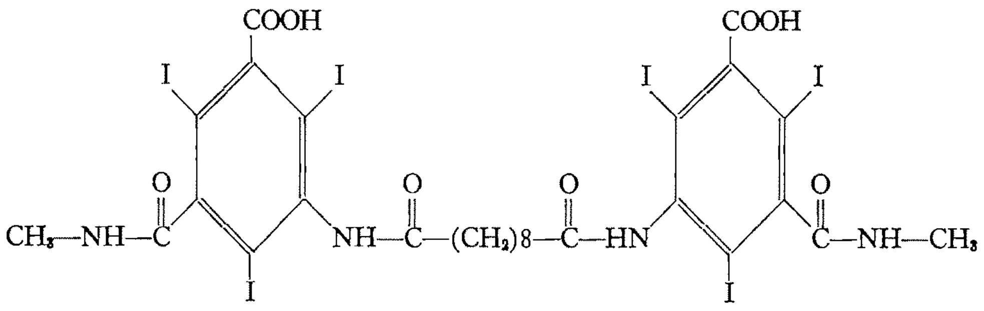
Comparative intravenous cholangiographic screening of MP-271 and iodipamide methylglucamine in cats at a dosage level of 64 mg. of iodine per kilogram of body weight revealed that the drugs compare favorably as agents for biliary tract visualization. In the cats iodipamide methylglucamine produced vomiting, while MP-271 exhibited no untoward effect. Comparative blood-brain-barrier studies were conducted in mongrel dogs with MP-271 and iodipamide methylglucamine. Doses of 5 cc. of iodipamide methylglucamine were found to be decidely more injurious to the blood-brain-barrier than a 20 cc. dose of MP-271. Chronic toxicity studies in rats and dogs indicate that MP-271 is not likely to produce toxic effects in the anticipated clinical dosage range of 200–300 mg./kg. These pharmacologic and toxicologic studies are reported in detail elsewhere.[1] On the basis of these data, a clinical study was initiated on January 14, 1963 to determine the optimum dosage,

---

* Mallinckrodt Chemical Works.

* From the Department of Radiology, University of Louisville School of Medicine, Louisville, Kentucky.

Aided in part by a grant from Mallinckrodt Chemical Works.



Empirical Formula $C_{28}H_{28}I_6N_4D_8$

Fig. 1.

rate of injection, pharmacologic action, toxicity, and usefulness of this new drug for intravenous cholangiography.

METHOD AND PROCEDURE

MP-271 has been employed as the contrast medium for intravenous cholangiographic studies in 50 patients at the time of this writing. Each patient was questioned for a history of allergy or iodine sensitivity and 1 cc. of MP-271 was injected intradermally followed by a 1 cc. test dose given intravenously. Thirty-five patients received 20 cc. and 15 patients received 30 cc. of MP-271. An anteroposterior 20 degree right posterior oblique scout roentgenogram of the right upper quadrant was taken prior to injection. Following injection, roentgenograms were made every 10 minutes for 1 hour to demonstrate the bile ducts, and at 2, 3, and 24 hours. In some patients with good gallbladder visualization, a fatty meal was administered and a roentgenogram was made at 30 minutes to study the contraction of the gallbladder. When indicated, laminagrams of the common duct were obtained.

A bromsulphalein test, blood urea nitrogen and blood creatinine were obtained prior to injection in every patient and a repeat blood urea nitrogen and blood creatinine were obtained 2 days after injection. At 1 month the bromsulphalein test, blood urea nitrogen and blood creatinine were repeated. All patients have had one or more routine urinalyses and blood counts. Serum bilirubin determinations were obtained on 20 of the patients prior to injection during the course of this study. Further progress studies on these patients are being carried out for signs of delayed toxicity.

ACTION

Ten to thirty minutes following the injection of MP-271, contrast material was seen in the kidneys and urinary bladder of 45 of the 50 patients studied, with maximum visualization occurring at 20 minutes (Fig. 2). After this time, excretion by the kidneys decreased. Visualization of the common duct occurred between 10 to 15 minutes after injection with maximum visualization occurring around 50 minutes.

Table II

ANIMAL TOXICITY STUDIES[3]

Acute Toxicity	MP-271	Iodipamide Methylglucamine
(a) Intravenous LD_{50} (mice)	13,100 mg./kg. (10,800–15,900)	4,120 mg./kg. (3,120–4,890)
(b) Intracerebral LD_{50} (mice)	1,120 mg./kg. (est.)	62.1 mg./kg. (41.1–93.7)
(c) Intravenous LD_{50} (rats)	6,600 mg./kg. (6,110–7,130)	
(d) Intravenous LD_{50} (dogs)	10,000 mg./kg.	

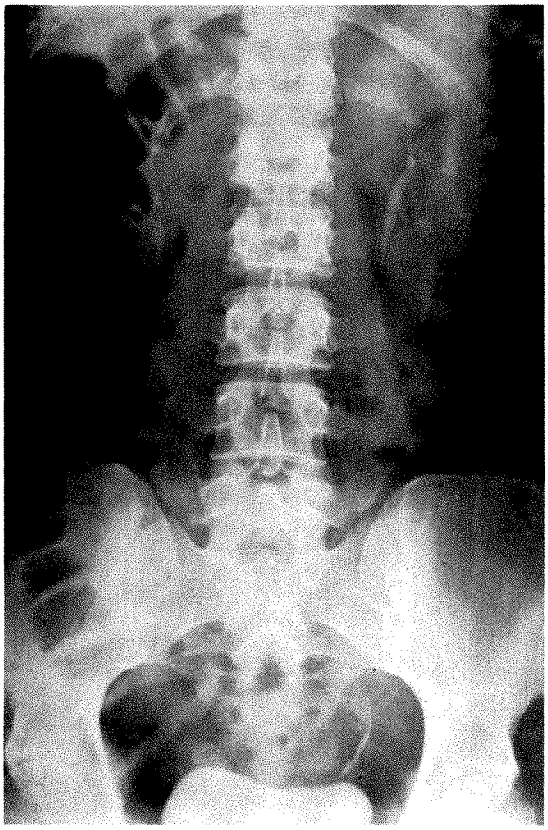


FIG. 2. Roentgenogram 20 minutes after the injection of 20 cc. of MP-271 showing maximum excretion by the kidneys.

The gallbladder began to visualize at about 50 minutes to 2 hours after injection with maximum visualization (Fig. 3) at 3 hours. In many patients excellent visualization of the gallbladder was present at 24 hours and in many cases the visualization was better at this time than that which occurred at 1 to 3 hours (Table III).

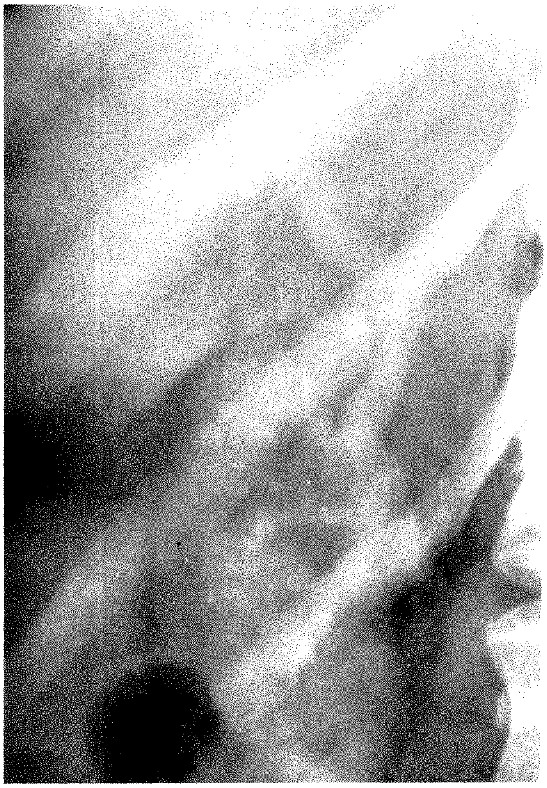


FIG. 3. Normal common duct in a patient who had nonvisualization of the gallbladder with a double dose of an oral contrast medium. Contrast material can be seen in the kidney 50 minutes after the intravenous injection of 20 cc. of MP-271.

In some patients with good visualization of the gallbladder at 24 hours, a large amount of contrast material was seen in the gastrointestinal tract (Fig. 4). This indicated that the greater proportion of this material was being excreted through the bile ducts while the early kidney roentgenograms indicated that a lesser amount was eliminated through the urinary tract.

TABLE III

TIME OF MAXIMUM VISUALIZATION WITH MP-271 IN 50 PATIENTS

Visualization	Minutes						Hours		
	10	20	30	40	50	60	2	3	24
Ducts			3	15	23	4	2		
Gallbladder					3	1	1	16	9
Kidneys	10	20	15						

VISUALIZATION OF DUCTS AND GALLBLADDER

In this series of 50 patients, visualization of the ducts occurred in 47 (94.0 per cent) patients (Table IV). In 35 patients who had no previous gallbladder surgery, 33 (94.3 per cent) had visualization of the ducts and 30 (85.7 per cent) had visualization of the gallbladder and ducts. Wise and O'Brien[5] found that with iodipamide methylglucamine visualization of the ducts occurred in 97 (88.8 per cent) of 109 patients with no previous gallbladder surgery. These figures indicate the possibility for obtaining a slightly higher percentage of duct visualization in noncholecystectomized patients with MP-271 as opposed to iodipamide methylglucamine.

SIDE EFFECTS

No mortality or serious reactions have occurred in our series of 50 patients. Neither have local reactions at the site of injection nor urticaria or other skin eruptions been observed. Nausea and vomiting were experienced by only 2 patients. In 1 of these patients, the serum bilirubin was 3.4 mg. per cent.

It was noticed that MP-271 could be injected much more rapidly than iodipamide methylglucamine without causing nausea. Although MP-271 is slightly more viscous than iodipamide methylglucamine, this was felt to be of no particular disadvantage. Most of the patients received the total injection within $1\frac{1}{2}$ to 5 minutes and some were injected over a period of 10 minutes. The optimum rate of injection appears to be in the 3 to 5 minute range.

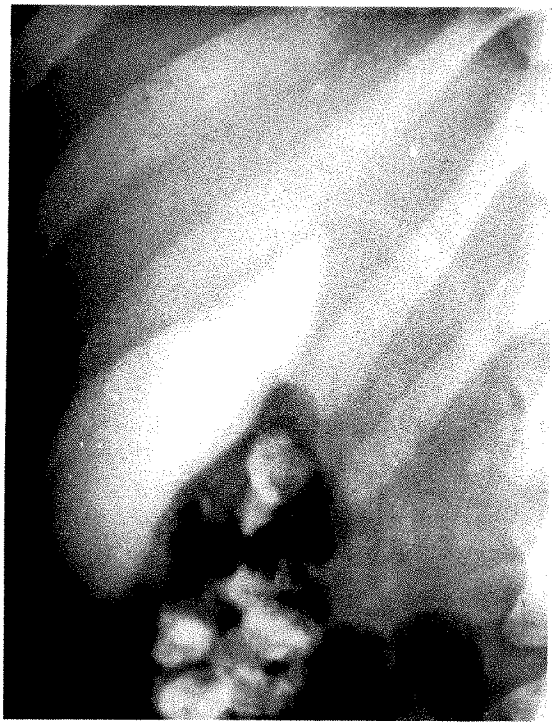


Fig. 4. Extent of visualization of the gallbladder and cystic duct 24 hours after the injection of 20 cc. of MP-271. Some of the contrast medium can be seen in the colon.

No patient tested 2 days post injection has shown any significant elevation of either the blood urea nitrogen or blood creatinine levels when compared to the control values. On the basis of laboratory studies carried out on 25 patients at 1 month post injection, there is no evidence to indicate that MP-271 has aggravated or initiated liver damage. These studies are continuing. No change has been noted in blood pressure determinations.

Table IV

RESULTS OBTAINED WITH MP-271 IN 50 PATIENTS

Patient Classification	No.	Visualization of Ducts	Visualization of Gallbladder and Ducts
Cholecystectomized	15	14 (93.3%)	
Not Cholecystectomized	35	33 (94.3%)	30 (85.7%)
Patient Total	50	47 (94.0%)	

DISCUSSION

This study indicates the usefulness of a 75 per cent w/v solution of the N-methylglucamine salt of 5,5′-sebacoyl-diimino-bis (2,4,6-triiodo-N-methylisophthalamic acid) as an intravenous cholangiographic contrast medium. Visualization of the biliary ducts occurred in 47 (94.0 per cent) out of 50 patients. This is considered to be a high incidence of visualization for an intravenous cholangiographic agent.[2,4]

In 10 patients with previous nonvisualization of the gallbladder with a double dose of iopanoic acid, a follow-up examination with MP-271 produced duct visualization in 70.0 per cent of the patients. In 1 of these patients there was excellent demonstration of the common duct with evidence of small nonopaque stones in the gallbladder and common duct, and dilatation of the common duct.

Serum bilirubin determinations were obtained in 20 of the 47 patients with adequate biliary tract visualization. In 15 (75.0 per cent) of these patients the levels were below 3 mg. per cent and in 5 (25.0 per cent) the levels were above 3 mg. per cent. There was excellent visualization of the ducts in 2 of the patients with clinical jaundice and serum bilirubin values between 3.5–4.5 mg. per cent. Both of these patients had significant bromsulphalein retention.

Cross-over studies using iodipamide methylglucamine are in progress and these results will be reported at a later date.

SUMMARY AND CONCLUSIONS

Preliminary clinical studies have been conducted with MP-271, a promising new intravenous cholangiographic medium. Visualization of the biliary ducts was demonstrated in 47 (94.0 per cent) out of 50 patients and visualization of the gallbladder and ducts in 30 (85.7 per cent) of the 35 noncholecystectomized patients. Maximum opacification of the ducts occurred in 50 minutes and of the gallbladder in 3 hours. There appears to be a higher degree of kidney excretion with MP-271 than is commonly seen with iodipamide methylglucamine, with the maximum excretion occurring at 20 minutes.

A dose of 20 cc. appears to be adequate for visualization of the biliary ducts in adults. It appears that MP-271 can be injected much more rapidly than iodipamide methylglucamine without increasing the incidence of side effects. Only 2 instances of nausea and vomiting have been encountered in this series of 50 patients. No evidence of hepatic or renal damage attributable to MP-271 has been detected by our laboratory studies. On the basis of these studies, MP-271 would appear to be a highly efficient and well tolerated contrast medium.

Thomas R. Marshall, M.D.
Department of Radiology
University of Louisville
School of Medicine
Louisville 2, Kentucky

The author is grateful to Mr. Frank Zeloski, Clinical Development Department, Mallinckrodt Pharmaceuticals and Miss Marty Schan for aid in preparation of the manuscript.

REFERENCES

1. BAEDER, D., TUSING, T., BEN, M., and BUTLER, W. Pharmacology and Toxicology of MP-271. Scientific Paper presented before the 47th Annual Meeting of Federation of American Societies for Experimental Biology, Atlantic City, New Jersey, April, 1963. To be published.
2. JOHNSON, G., JR., PEARCE, C., and GLENN, F. Intravenous cholangiography in biliary tract disease. *Ann. Surg.*, 1960, *152*, 91–102.
3. Mallinckrodt Pharmaceuticals. Clinical Research Data Sheet, Jan. 9, 1963.
4. Preliminary report to Mallinckrodt Chemical Works, March 12, 1963 by MARSHALL, T. R.
5. WISE, R. E., and O'BRIEN, R. G. Interpretation of intravenous cholangiogram. *J.A.M.A.*, 1956, *160*, 819–827.

Vol. 90, No. 4

RENAL INSUFFICIENCY FOLLOWING CHOLECYSTOGRAPHY*

By WILLIAM B. SEAMAN, M.D., STUART COSGRIFF, M.D., *and* JOSEPHINE WELLS, M.D.
NEW YORK, NEW YORK

CHOLECYSTOGRAPHY, a widely used diagnostic examination, is usually considered a relatively benign procedure; however, the minor side effect of acute diarrhea in a debilitated patient is an undesirable burden, particularly if the examination is not absolutely necessary for the patient's care.

A more serious complication, acute renal insufficiency, with cholecystography has been reported several times in the medical literature, in 2 instances with fatal termination.[2,5,6,12] This complication, following both bunamiodyl* and iopanoic acid,† occurred in each case when more than the usual single dose was given. Our recent experience with such a complication of transient renal insufficiency has prompted this report and a review of the literature.

REPORT OF A CASE

A 52 year old female (146-71-20) with a history of alcoholism entered the hospital with a chief complaint of low grade fever. Four months previously she had had an upper respiratory infection which had responded to antibiotics. Significant laboratory findings noted elsewhere prior to hospital admission included a urinalysis that was negative except for a rare white blood cell on microscopic examination, cephalin flocculation 4+, serum bilirubin 1.2 mg. per cent, serum albumin 4.4 gm. per cent, and serum globulin 2.7 gm. per cent.

On admission the positive findings were low grade fever and firm hepatomegaly, the lower border of the liver extending 5 cm. beneath the costal margin. Urinalysis revealed a specific gravity of 1.015, one plus albuminuria (sulfosalicylic acid method), an occasional white blood cell and no casts on microscopic examination. Other pertinent laboratory data included: sedimentation rate (Westergren) 17 mm./hour; bromsulphalein retention 90 per cent at 5 minutes, 43 per cent at 30 minutes; bilirubin 2.1 mg. per cent; negative cephalin flocculation; hemoglobin 12.0 gm.; red blood cell count 4.32 million; white blood cell count 10,000 with a normal differential; serum protein electrophoretic pattern showed albumin 2.9 gm. per cent; total globulin 2.9 gm. per cent of which gamma globulin was 1.1 gm. per cent; alkaline phosphatase level 29 King-Armstrong units; prothrombin time 15 seconds (normal 14).

On the day of admission (March 5, 1960) she was given 3 gm. (6 tablets) of iopanoic acid. Since this did not result in gallbladder visualization, the following day 6 gm. (12 tablets) of iopanoic acid was administered, resulting in faint opacification of the gallbladder without evidence of stones.

On March 15, 1960 because of possible mild ascites she was started on 50 mg. of hydrodiuril daily, which was continued for the subsequent 15 days. On March 29, 1960, twenty-two days after her second cholecystography, when her liver function tests had shown some favorable changes (serum albumin from 2.9 to 3.8 gm. per cent, bilirubin from 2.1 to 1.2 mg. per cent, alkaline phosphatase 29 to 25 King-Armstrong units), she was given 9 gm. (12 capsules) of bunamiodyl which resulted in faint gallbladder opacification. She experienced diarrhea, but less than with iopanoic acid. There was accompanying abdominal discomfort, mild nausea, and several episodes of retching. She did not appear dehydrated.

On the day following cholecystography, she reported passing "a scant amount of urine" during the preceding 36 hours. She appeared comfortable and well, not dehydrated; her blood pressure was normal. Only 5 cc. of urine was voided in the subsequent 18 hours. This specimen contained 4+ albumin (sulfosalicylic acid), many white blood cells, and 3-4 granular casts per high power field. During the following day,

---

* Bunamiodyl=orabilex.

† Iopanoic acid=telepaque.

* From the Departments of Radiology and Medicine, Columbia University, College of Physicians and Surgeons and the Presbyterian Hospital, New York, New York.

(April 1, 1960) the urine output was 70 cc. with a specific gravity of 1.015 and 4+ albumin with "much debris" seen on microscopic examination. The urea nitrogen rose from 33 mg. per cent on this day, to 113 mg. per cent 2 days later. On that day, April 3, 1960, the urine output was 725 cc. and subsequently increased even further. Thereafter the blood urea nitrogen gradually fell, reaching 11 mg. per cent on the ninth day (April 9, 1960). At that time the urinalysis was negative for albumin, although 1+ albuminuria was seen on the next two days.

Two months later, re-evaluation was carried out. At that time two urinalyses were done and showed a specific gravity of 1.014 and 1.016 respectively with no albumin and an occasional white blood cell; the blood urea nitrogen was 8 mg. per cent. Other laboratory observations at this time were alkaline phosphatase 11 King-Armstrong units, cephalin flocculation test 2+, and bromsulphalein 39 per cent retention at 30 minutes.

She was re-admitted to the hospital for a check-up examination one year later when the significant laboratory findings included: phenolsulfonphthalein excretion of 87 per cent in 2 hours, urea nitrogen 16 mg. per cent, alkaline phosphatase 21 King-Armstrong units, bromsulphalein retention of 17 per cent at 30 minutes and an equivocal cephalin flocculation test. At this time the urinalysis was completely negative on two specimens with specific gravity of 1.020, urine concentration test to 1.028.

COMMENT

It was the opinion of the physicians who saw her that this episode represented a toxic renal parenchymal disorder. The possibility that vomiting and diarrhea had resulted in severe dehydration and renal damage seemed unlikely, as did the possibility that the preceding diuril administration produced more than a minor degree of nitrogen retention. The presence of 1+ albuminuria found in the urinalysis performed at the time of hospital entry suggested the possibility of underlying chronic renal disease. However, this seemed unlikely in view of the fact that additional urinalyses done prior to her hospital admission and subsequent to her recovery showed no albuminuria. Although a blood urea nitrogen was not determined as part of the initial workup in the hospital, the subsequent return of the blood urea nitrogen to 11 mg. per cent 11 days after the episode of oliguria would suggest that her renal function was adequate.

Bunamiodyl, a tri-iodophenyl compound containing 57 per cent iodine, is largely excreted in the feces. According to Lasser *et al.*,[8] about 75 per cent is excreted in the feces and 25 per cent in the urine. Although dysuria occurs following the ingestion of cholecystographic media, the incidence is only 1–3 per cent after bunamiodyl as compared to 9 per cent following iopanoic acid.[18]

Practically all of the known compounds used for oral cholecystography are readily precipitated by acidification and thus may give rise to false positive tests for protein when the urine is tested with acid reagents such as Exton's (sulfosalicylic acid) or Roberts' (nitric acid). Thus it is possible that the positive tests for urinary protein may actually have represented a pseudoalbuminuria. Since the latter rarely lasts over 2 to 3 days, it is unlikely that this phenomenon explains all of the positive urine tests for protein in this patient.[7,10,13,14,15]

In contrast to the parenteral administration of organic iodine compound for roentgenographic purposes, serious reactions after oral administration are virtually unknown. Following oral cholecystography it is well known that side reactions such as abdominal cramps, diarrhea, dysuria, headache, nausea, vomiting, dizziness, and rarely urticaria may occur. Only 2 cases of severe allergic reactions after oral administration of cholecystographic media (iodoalphionic acid) have been reported, 1 of which occurred after a double dose.[4,16] Littmann and Marcus[9] described 4 cases of coronary occlusion occurring within hours following the oral administration of the cholecystographic drug but the relationship is obscure.

In cats, nephrotoxicity has been demonstrated following the oral administration of iodoalphionic acid (priodax). Modell[11] de-

TABLE I

URINARY COMPLICATIONS FOLLOWING CHOLECYSTOGRAPHY

Author	Age	Sex	Dose	Drug	History of Renal Disease	Evidence of Liver Disease	Visualization	Remarks
Rene and Mellinkoff[12]	42	M	6 gm.	Iopanoic acid	Albuminuria 15 yr. before; urinalysis negative	Hepatitis 5 yr. before; exposure to CCl_4	Poor	Oliguria; 325 cc., 74 hr. BUN 64.5 mg. per cent; recovery 1 week
Rene and Mellinkoff[12]	60	F	3 gm. 6 gm.	Bunamiodyl; Iopanoic acid	Pyelonephritis 26 yr. before; urinalysis negative	None	None	
Blythe and Woods[2]	74	F	9 gm.	Bunamiodyl	Urinalysis negative	None	None	11th day, oliguria; 5th day, 20 cc.
Gunn[6]	63	M	6.75 gm. 6.75 gm.	Bunamiodyl Bunamiodyl	Urgency 2 yrs.; urinalysis negative	None	None	
Gunn[6]	69	F	4.5 gm.; 9 gm. and 9 gm. next day	Bunamiodyl	2+ albumin; red and white blood cells	None	None	Death
Gunn[6]	73	F	4.5 gm.; 9 gm.	Bunamiodyl	Urinalysis negative	None	None	Oliguria and elevated BUN
Seaman, Cosgriff and Wells	52	F	9 gm.	Bunamiodyl	None	Fatty liver; Laennec's cirrhosis	Faint	Oliguria and elevated BUN
Gottlieb, Spiera and Gordis[5]	43	F	9 gm.	Bunamiodyl	None	Jaundice		Oliguria 16 days; BUN 270 mg. per cent; death
Gottlieb, Spiera and Gordis[5]	55	M	9 gm.	Bunamiodyl	None	Jaundice; hepatitis		Oliguria and BUN 90 mg. per cent; spontaneous recovery

scribed albuminuria lasting 1 to 7 days in all of the 7 cats receiving 500 mg. doses and in 3 of 5 cats receiving 100 to 500 mg. orally. In 2 animals that expired, large pale kidneys with cloudy swelling of the tubule cells were demonstrated.

More recently, there have been several reports of acute renal insufficiency complicating oral cholecystography and these are summarized in Table I. It is of interest to note that all have been associated with the administration of more than the usual single dose and there is little evidence to suggest pre-existing renal disease. One patient had had albuminuria 15 years before but the recent examination was negative. Another had a history of pyelonephritis 26 years previously with a recent normal urinalysis. One of Gunn's cases[6] (No. 5) initially had a 2+ albuminuria and a blood urea nitrogen of 29 mg. per cent. However, in 4 cases, including the patient herein reported, there was some evidence of liver damage. The existence of a possible competitive mechanism for the excretion of halogenated aromatic compounds is suggested by reports that the administration of bunamiodyl results in bromsulphalein retention and interferes with bilirubin excretion.[3,17] It is possible that impaired hepatic function might have played a role by increasing the amount of cholecystographic material presented to the kidneys for excretion. The patient reported herein had considerable hepatomegaly, considered to be a fatty liver and cirrhosis secondary to alcohol. In the case reports in which a statement about the gallbladder visualization was made, visualization of the gallbladder was not normal. On the other hand, Bickham *et al.*[1] gave 9 gm. of bunamiodyl to 40 patients with nonvisualization of the gallbladder after 4.5 gm. and did not note any urinary complications.

Although it is difficult to draw any conclusions from such a limited experience, the existing available evidence suggests that large doses of cholecystographic agents should be used with caution, especially in patients with signs of hepatic damage. In 7 of the 9 patients, the associated drug was bunamiodyl, although in 1 patient iopanoic acid was used and another patient received both agents. It is conceivable that lesser degrees of transient oliguria and azotemia following cholecystography might be overlooked due to the absence of clinical symptoms.

SUMMARY

A case of acute renal insufficiency with recovery following oral cholecystography (with bunamiodyl) is reported. A review of the medical literature has disclosed 8 additional cases including 2 fatalities. All of the reported cases occurred after more than the usual single dose of contrast material. The presence of significant hepatic or renal disease warrants caution in the use of large doses of cholecystographic media.

William B. Seaman, M.D.
Columbia-Presbyterian Medical Center
622 West 168th Street
New York 32, New York

REFERENCES

1. Bickham, C. E., Jr., Wissler, J. E., Schumacher, F. W., and Miele, A. J. New contrast medium for oral cholecystography and cholangiography. Exhibit presented at the Scientific Session of A.M.A., Atlantic City, June, 1959.
2. Blythe, W. B., and Woods, J. W. Acute renal insufficiency after ingestion of gall-bladder dye. *New England J. Med.*, 1961, *264*, 1045–1046.
3. Bolt, R. J., Dillon, R. S., and Pollard, H. M. Interference with bilirubin excretion by gallbladder dye (bunamiodyl). *New England J. Med.*, 1961, *264*, 550–552.
4. Cohen, S. G., Armen, R. N., and Kantor, M. Anaphylactoid reaction following oral administration of iodide-containing cholecystographic media. *J. Allergy*, 1956, *27*, 544–547.
5. Gottlieb, A., Spiera, H., and Gordis, E. Fatal renal insufficiency following oral cholecystography. *New England J. Med.*, 1962, *267*, 389–392.
6. Gunn, J. A. Urinary complications following bunamiodyl. *J.A.M.A.*, 1961, *175*, 911–912.
7. Holoubek, J. E., Carroll, W. H., Riley, G. M., and Langford, R. B. Evaluation of pseudoalbuminuria following cholecystography in 76 cases. *J.A.M.A.*, 1953, *153*, 1018.
8. Lasser, E. C., Meadows, P. M., Granke, R. C., and Feist, J. H. Some observations of absorption and excretion of bunamiodyl (orabilex) in man. *J. Nuclear Med.*, 1960, *1*, 79–82.
9. Littmann, D., and Marcus, F. I. Coronary insufficiency associated with oral administration of gall-bladder dye. *New England J. Med.*, 1958, *258*, 1248–1250.
10. Mark, L. K., Moel, M., Enzer, N., and Volk, E. Orabilex and pseudoalbuminuria. *Radiology*, 1960, *75*, 954.
11. Modell, W. Pharmacology of β(3,5 di-iodo-4-hydroxyphenyl): A phenyl propionic acid. *J. Lab. & Clin. Med.*, 1942, *27*, 1376–1384.
12. Rene, R. M., and Mellinkoff, S. M. Renal insufficiency after oral administration of double dose of cholecystographic medium. *New England J. Med.*, 1959, *261*, 589–592.
13. Seedorf, E. E., Powell, W. N., Greenlee, R. G., and Dysart, D. N. Telepaque and pseudoalbuminuria. *J.A.M.A.*, 1953, *152*, 1332–1333.
14. Seedorf, E. E., Powell, W. N., Greenlee, R. G., and Hartman, J. T. Priodax and pseudoalbuminuria. *Radiology*, 1950, *55*, 740–742.
15. Seedorf, E. E., Powell, W. N., Greenlee, R. G., and Dysart, D. N. Pseudo-albuminuria following monophen and priodax. *Radiology*, 1952, *59*, 422–423.
16. Sheldon, J. M., and Lovell, R. G. Asthma due to halogens. *Am. Pract.*, 1949, *4*, 43–44.
17. Shotton, D., Carpenter, M., and Rinehart, W. B. Bromsulfalein retention due to administration of gall-bladder dye (bunamiodyl). *New England J. Med.*, 1961, *264*, 550–552.
18. Whitehouse, W. M., and Fink, H. E., Jr. Controlled comparative statistical study of orabilex and telepaque in cholecystography. *Univ. Michigan M. Bull.*, 1959, *25*, 238–242.

SPATIAL FLUCTUATIONS OF X-RAY QUANTA AND THE RECORDING OF RADIOGRAPHIC MOTTLE*

By K. ROSSMANN, PH.D.
ROCHESTER, NEW YORK

THE purpose of the radiographic screen–film system is the recording of information which arrives at the system in the form of a certain distribution of x-ray quanta in space. This distribution is determined by the configuration and composition of the object being radiographed and by the energy of the x-ray quanta used. During the transfer of information through the system, many processes, such as energy conversion, amplification, and imaging,[4] take place, all of which affect the final record of the information which is in the form of a metallic silver deposit on a flexible support.

Like all information-transmitting and -recording systems, the screen–film system has certain inherent imperfections which limit its capacity to transfer all the information which is put into it and which, therefore, reduce its usefulness. It is the task of the designer of the system to create the best possible configuration of components, *i.e.*, one which reduces the imperfections to a minimum. To this end, a thorough study has to be made of all factors which affect system performance.

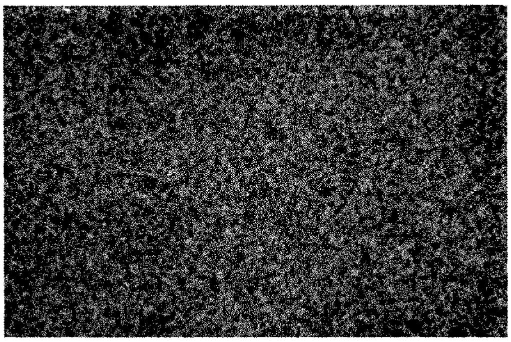


FIG. 1. Mottle of a radiograph made with intensifying screens.

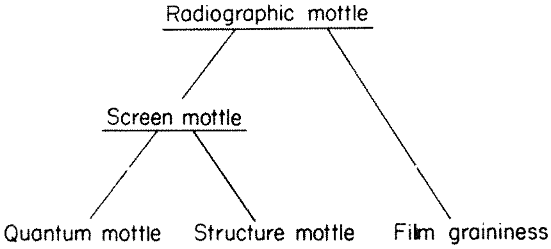


FIG. 2. The components of the coarse density fluctuations observed on x-ray films exposed with fluorescent screens (radiographic mottle).

Of major importance among these factors in the screen–film system is the mottle of the radiograph, because it reduces detail visibility and is also esthetically disturbing. We define* the term *radiographic mottle* to mean the impression gained by an observer when looking at the radiograph shown in Figure 1, for example,† which was obtained by exposing a medium-speed screen–film system to a uniform beam of x-rays ("flash exposure"). It is well known[1] from experimental investigations that radiographic mottle consists of several components, as outlined in Figure 2. First, a coarse density fluctuation results from spatial fluctuations of the x-ray quanta absorbed in the screens. We have called this density fluctuation *quantum mottle*. Second, structural inhomogeneities in the phosphor coating of the screens can cause a density fluctuation called *structure mottle*. In cases where both of these phenomena are present we shall denote their combined effect as *screen mottle*. However, in modern intensify-

---

* The nomenclature introduced in this paper is an improvement over that used in earlier publications.[1,2,3] The authors of these earlier papers have collaborated in the revision.

† In this and subsequent illustrations of mottle, a magnification of 2× and increased contrast were used to make a satisfactory halftone reproduction.

* Communication No. 2335 from the Kodak Research Laboratories, Eastman Kodak Company, Rochester, New York.
Read in part at the Tenth International Congress of Radiology, Montreal, Quebec, Canada, August 26–September 1, 1962, under the title: "Application of Communication Theory to Medical Radiography."

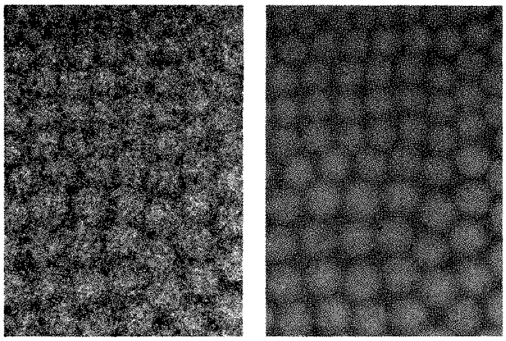


Fig. 3. The effect of radiographic mottle on the visibility of low-contrast detail. *Left:* radiograph made with a medium-speed screen–film system. *Right:* radiograph made with a 200-times slower screen–film system (same screens as on the left).

ing screens, structure mottle is normally very small relative to quantum mottle. It will, therefore, not be investigated further in what follows. The third component of radiographic mottle is *film graininess*, which is due to the built-in random distribution of exposed grains in the emulsion. Film graininess also is usually negligible relative to quantum mottle. It will, however, be included in the subsequent theoretic considerations because it forms an important part of experiments which illustrate and support the theoretic findings. Thus, the coarse variation in density seen on radiographs made with intensifying screens (radiographic mottle) is due primarily to the spatial fluctuations of the x-ray quanta absorbed in the screens. Where the meaning is clear, we shall, for the sake of brevity, refer to radiographic mottle simply as "mottle."

The effect of mottle on the visibility of low-contrast detail is illustrated in Figure 3, which shows two radiographs of plastic beads obtained with the same intensifying screens and kilovoltage, but using different films. Although sharpness, contrast, and film graininess of the two films were not identical, by far the most significant difference between the two systems was speed, the one showing coarser mottle being 200 times faster than the other one. Thus, it is seen that mottle can, under certain conditions, markedly reduce the information content of a radiograph.

The origin and effect of this mottle have been studied by Sturm and Morgan,[5] who applied statistical principles to determine the spatial distribution of the exposing x-ray quanta and, from this, drew conclusions regarding the fluctuation of light quanta seen by the eye of a person viewing a radiograph. However, their derivations are quite general because they are intended to apply to many types of radiologic image-forming systems and, thus, do not specifically take account of characteristic parameters of screen–film systems, such as film graininess and film contrast, for example. It is of interest to carry out an analysis of this kind for screen–film systems and to show that purely statistical methods, *i.e.*, methods involving only the *number of quanta* involved, are inadequate for the explanation of many observed phenomena.

As stated previously, when modern screens are used, the mottle of radiographs made with fluorescent screens consists of two components, film graininess and quantum mottle. It is convenient to describe these in terms of the standard deviation of the corresponding density fluctuation, $\sigma(D)_{\text{grain}}$ and $\sigma(D)_{\text{mottle}}$, respectively. Since film graininess and quantum mottle are independent random spatial phenomena, the standard deviation of the total radiographic mottle resulting from their superposition can be written*

$$\sigma(D)_{\text{total}} = [\sigma^2(D)_{\text{grain}} + \sigma^2(D)_{\text{mottle}}]^{1/2}. \quad (1)$$

The physical meaning of $\sigma(D)_{\text{total}}$ can be stated as follows: If a densitometer trace of the uniformly exposed and developed radiograph is made, approximately 68 per cent of all measured densities will lie within a density range $\overline{D} \pm \sigma(D)_{\text{total}}$, where $\overline{D}$ is the average density of the radiograph. The mottle component, $\sigma(D)_{\text{mottle}}$, can be expressed in terms of the number of x-ray quanta absorbed in the screens during the exposure as follows.

---

* In systems where structure mottle is not negligible, a term $\sigma^2(D)_{\text{structure}}$ would have to be added inside the brackets, if the phenomenon is random.

Let us assume that the number of x-ray quanta absorbed per unit area of the screen is n_x. Then the number absorbed in some area element a, equal to the area of the scanning or viewing aperture, is $n_x a$. This number fluctuates randomly about an average number $\bar{n}_x a$, according to a Poisson distribution, similar to raindrops striking a pavement. The resulting standard deviation is given by

$$\sigma_x = \sqrt{\bar{n}_x a}. \qquad (2)$$

The corresponding fluctuation of photographic density, ΔD_{mottle}, from area to area can be found by combining equation (2) with the expression for the characteristic curve of the film which is, for small exposure intervals, ΔE,

$$D = G \log E + C,$$

where G is the gradient of the film and C is the fog plus base density. Then

$$\Delta D = 0.43 G \frac{\Delta E}{\bar{E}} = 0.43 G \frac{\sigma_x}{\bar{n}_x a}$$

and, substituting from equation (2),

$$\sigma(D)_{\text{mottle}} = 0.43 G \frac{1}{\sqrt{\bar{n}_x a}} \cdot$$

Substituting into equation (1), we obtain

$$\sigma(D)_{\text{total}} = \left[\sigma^2(D)_{\text{grain}} + (0.43G)^2 \frac{1}{\bar{n}_x a} \right]^{1/2} \cdot \qquad (3)$$

This equation, which was derived by taking into consideration only the number of x-ray quanta required to make a radiograph, shows that $\sigma(D)_{\text{total}}$ increases as the number of x-ray quanta absorbed in the screens during the exposure decreases. Thus, it explains very well the increase of mottle with speed of the system. However, there are phenomena which it does not explain.

For example, Figure 4 shows a series of flash-exposure radiographs made with the same number of x-ray quanta. According to the purely statistical result given by equation (3), all the radiographs should show the same mottle. This is obviously not the case. The most pronounced mottle was obtained by having screen and film in intimate contact. The introduction of an increasing space between screen and film decreased the mottle until, finally, only the film graininess remained. Spacing of screen and film altered the optical characteristics of the screen–film system by increasing the light diffusion, while other parameters, such as speed, were kept constant. It is seen from the figure that, during this process, the mottle changed its appearance from fine and sharp to coarse and diffuse, and then to the very fine and sharp film graininess. Although screens and film are not usually spaced apart, analogous changes of optical

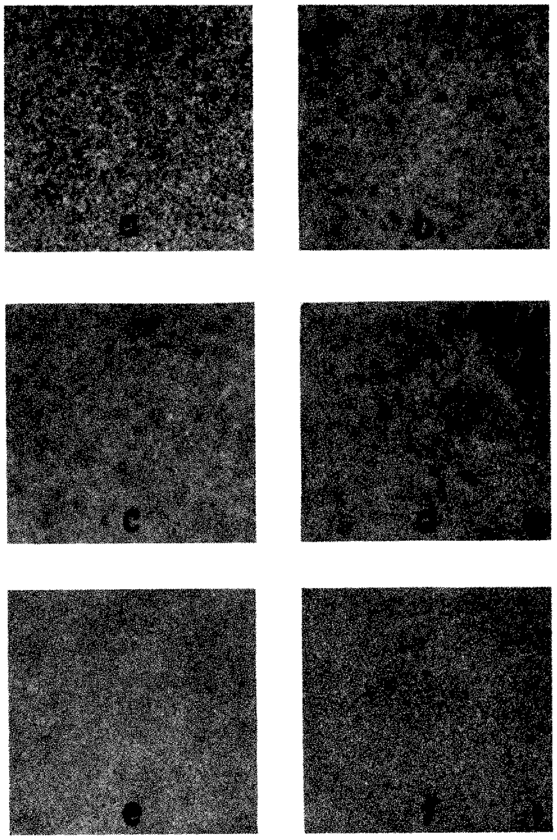


Fig. 4. Radiographic mottle. An air space of increasing width was introduced between screen and film: (*a*) intimate contact, (*b*) 0.02 mm., (*c*) 0.05 mm., (*d*) 0.12 mm., (*e*) 0.23 mm., and (*f*) 13.0 mm.

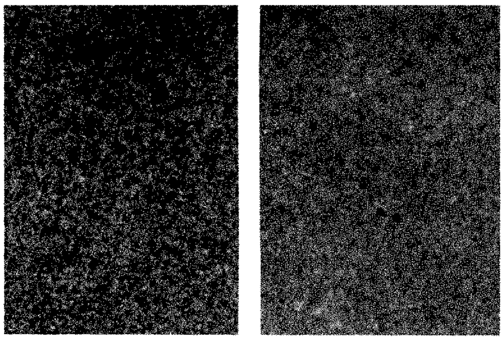


Fig. 5. Radiographic mottle. *Left:* slow screen (calcium tungstate). *Right:* fast screen (barium lead sulfate).

characteristics are obtained in practice through differences in screen thickness or phosphor material. However, in these cases, complications are introduced by simultaneous changes of system speed. The spacing experiment serves to illustrate the dependence of mottle on the optical properties alone, by eliminating all other variables.

A second example of the inadequacy of the purely statistical method is presented in Figure 5, which shows radiographs made with a slow screen and a fast screen on the same kind of film. During the exposure the slow screen absorbed 1.5 times the number of x-ray quanta absorbed by the fast screen, to give the same density on the film. According to equation (3), the mottle of the slow system should be less than that of the fast system. Instead, two completely different types of mottle were obtained, one being sharp and fine, the other coarse and diffuse. Although not all observers have the same preference, the mottle due to the fast system is less objectionable according to many observers.

The disagreement between theory and experiment can be resolved by considering the complete transfer characteristics of the screen–film system, and by the application of some concepts of statistical communication theory. In other words, it has to be taken into account that the screen–film system is not only an amplifier but is also an imperfect image-forming device, as indicated in Figure 6. The Poisson distribution of absorbed x-ray quanta will be regarded as an input to the system and, after modulation by the system and addition of the film grain pattern, the resulting density fluctuation as the output. The method by which the output is analyzed can be indicated by referring to more familiar communication systems which transmit information in the form of vibrations in time, with frequencies measured in cycles/sec. High-fidelity sound systems are a good example. It is common to evaluate the performance or transfer characteristics of such systems by comparing the power in the output vibrations with those in the input. If the vibrations are not simply sinusoidal, but are more complex and periodic, Fourier analysis can be used to separate the complex vibrations into sinusoidal components. By analogy, the random fluctuations of density which are the output of the screen–film system can be regarded as a composite of many sinusoidal frequencies, not in time, but in space, with frequencies measured in cycles/mm. The power in these fluctuations can be measured, frequency for frequency, by means of a microphotometer used in conjunction with a variable band-pass electronic filter and a true rms voltmeter.[2] The result is a power spectrum of the density fluctuations, as shown schematically by the curve marked Φ_{total} in Figure 7. The physical implications of this figure can be explained with the help of the mathematical representation of the power spectrum, which is[2]

$$\begin{aligned}\Phi(\nu)_{\text{total}} &= \Phi_{\text{grain}} + K\frac{G^2}{\bar{n}_x}\,|\,A(\nu)\,|^2 \qquad (4)\\ &= \Phi_{\text{grain}} + \Phi_{\text{mottle}},\end{aligned}$$

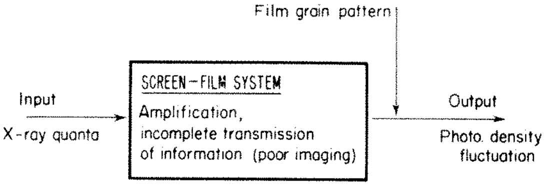


Fig. 6. Schematic representation of the screen–film system as an information-transmitting system.

where ν is the spatial frequency in cycles/mm., $|A^{\#}(\nu)|$ is the modulation transfer function* of the screen–film system, and K is a constant, which is independent of the system. This means that the power spectrum or spatial frequency content of the density fluctuations is dependent on the imaging properties of the system. For a perfect image-forming system we have $|A^{\#}(\nu)| \equiv 1$, so that

$$\Phi_{\text{perfect}} = \Phi_{\text{grain}} + K\frac{G^2}{\bar{n}_x},$$

which is the equation of the upper horizontal line in Figure 7. In other words, a perfect screen–film system transmits all frequencies with the same power, which depends only on the film grain pattern, on the film gradient G, and on the statistical average of the number of quanta absorbed per unit area of the screen during the exposure. The imperfect screen–film system, however, acts like a low-pass spatial frequency filter and does not transmit all spatial frequencies contained in the input, as shown by the curve marked Φ_{total} and equation (4). When screen and film are spaced sufficiently far apart so that no image is formed, then $|A^{\#}(\nu)| \equiv 0$ and $\Phi = \Phi_{\text{grain}}$, which is the equation of the lower horizontal line in Figure 7. The frequency ν_0 at which Φ_{total} merges with Φ_{grain} is an indication of the maximum resolution of the system, since, according to equation (4),

$$\Phi(\nu_0)_{\text{mottle}} = \Phi(\nu_0)_{\text{total}} - \Phi(\nu_0)_{\text{grain}} = 0$$

$$\text{implies } |A^{\#}(\nu_0)| = 0.$$

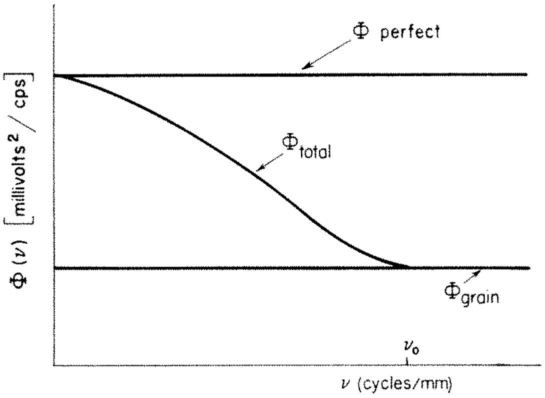


Fig. 7. Schematic illustration of power spectra of grain patterns. Φ_{perfect}—for a perfect screen–film system (theoretical); Φ_{total}—for a practical screen–film system; Φ_{grain}—for a film grain pattern.

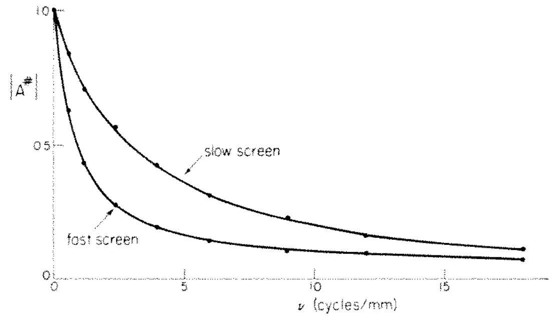


Fig. 8. Modulation transfer function of the slow (calcium tungstate) and fast (barium lead sulfate) screen–film systems used to make the radiographs shown in Figure 5.

The fact that the shape of the power spectrum of the density fluctuations depends on the modulation transfer function of the screen–film system suggests that the density fluctuations *can actually be used as a test pattern for the measurement of the modulation transfer function.*[2] This has been done with the help of equation (4), and Figure 8 shows the transfer functions of the same slow and fast screen–film systems which were used to make the flash-exposure radiographs in Figure 5. Since the same kind of film was used, the difference is due to the image-forming properties of the screens.

In order to obtain an expression for the standard deviation, $\sigma(D)_{\text{total}}$, of the density fluctuations which give the impression of mottle, we note that the area under the power spectrum curve equals the square of the standard deviation (variance). Thus, by substituting equation (4) into

$$\int_0^{\infty} \Phi(\nu)_{\text{total}} d\nu = \sigma^2(D)_{\text{total}}, \qquad (5)$$

---

* This term is now being used generally in place of what has been variously called "sine-wave response," "contrast transfer function," etc., in accordance with recommendations formulated in July, 1961 by the Subcommittee for Image Assessment Problems of the International Commission for Optics.

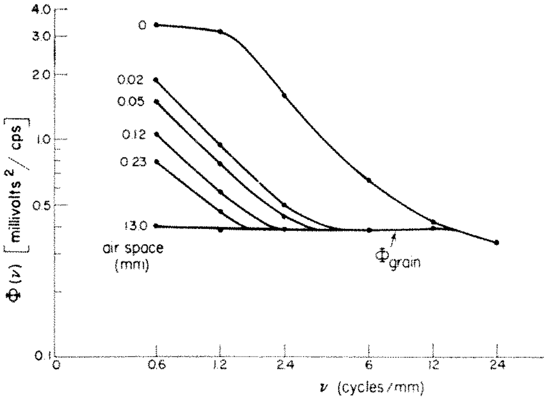


Fig. 9. Power spectra of the grain patterns obtained by introducing an air space of increasing width between screen and film (see Figure 4).

we obtain[3]

$$\sigma(D)_{\text{total}} = \left[\sigma^2(D)_{\text{grain}} + (0.43G)^2 \frac{1}{\bar{n}_x a} F^2\right]^{1/2} \qquad (6)$$

where $0 \leq F \leq 1$, and

$$F \rightarrow \begin{cases} 0 & \text{system unsharp (no imaging)} \\ 1 & \text{system sharp (perfect imaging).} \end{cases}$$

Note that $\sigma(D)_{\text{total}}$, obtained by the application of statistical communication theory and, therefore, also the mottle, depends not only on the number of absorbed x-ray quanta, but also on the image-forming, or optical, properties of the system through the function F. A system of poor image-forming quality can be expected to have less mottle than a sharp system, all other system parameters remaining the same. When this result is compared with equation (3), it is seen that the two equations become identical for perfect image-forming systems, *i.e.*, when $F=1$, and if the fluctuations due to the film grain pattern can be neglected.

The conclusions reached in the foregoing explain the phenomena illustrated in Figures 4 and 5. It will be recalled that the mottle series in Figure 4 was obtained with successively greater spaces between screen and film. When the power spectra of these grain patterns were measured, the curves in Figure 9 resulted. It is seen that, with increasing spacing, the point of intersection of Φ_{total} and Φ_{grain} moved to lower spatial frequencies, *i.e.*, the resolution of the systems decreased (spatial filtering). Simultaneously, the area bounded by Φ_{total} and Φ_{grain} decreased. This means, because of equations (5) and (6), that the mottle should change its appearance and that $\sigma(D)_{\text{total}}$ should decrease, which is in agreement with the visual impression gained from Figure 4.

This result implies that an analogous experiment could be performed with other radiologic image-forming systems which detect quantum noise. For example, in the case of television systems, narrowing of the amplifier bandwidth; in the case of fluoroscopic image amplifiers, the use of more highly diffusing screens; and for electro-optical systems, defocusing of the optics should have a similar effect on the appearance of the noise pattern.

The differences in the mottle obtained with a fast and a slow system, as shown in Figure 5, can be explained by means of Figure 8. It is apparent from the modulation transfer functions of the two systems that the fast screen does not resolve spatial frequencies as well as the slow screen and will, therefore, record a diffuse mottle pattern. Thus, according to equation (6), $\sigma(D)_{\text{total}}$ will be smaller for the fast system, which explains the fact that the mottle due to this particular fast system appears less objectionable than that of the slow system.

These results indicate that the mottle in radiographs made with intensifying screens is a complex phenomenon because it depends on the image-forming, or optical, characteristics of the screen–film system, as well as on the spatial fluctuations of the x-ray quanta. (Incidentally, this implies that $\sigma(D)_{\text{total}}$ does not represent a unique objective correlate to mottle in all cases, as discussed in another paper.[3]) Since earlier methods of analysis[5] yielded results which appear to be valid only for the special case of perfect image-forming systems, a re-examination of conclusions drawn from these earlier studies is needed. It is reasonable to assume that this is the case, not only for screen–film systems, but also, with the appropriate change of system parameters, for other radiologic image-forming systems which are sufficiently sensitive to detect the spatial fluctuations of the information-carrying quanta.

SUMMARY

The coarse density fluctuation (radiographic mottle) observed on high-speed x-ray films exposed with fluorescent intensifying screens arises primarily from statistical fluctuations in the spatial distribution of the absorbed x-ray quanta. Concepts of statistical communication theory have been used to develop a theory of radiographic mottle which is shown to be of more general validity than previous explanations. It is shown that the mottle depends not only on the number of x-ray quanta absorbed in the screens during the exposure but also on the image-forming, or optical, properties of the screen–film system. Experimental examples are given which substantiate the theory.

The results indicate that similar considerations should apply in the case of other radiologic image-forming systems which detect the spatial fluctuations of the information-carrying x-ray quanta.

Research Laboratories
Eastman Kodak Company
Rochester 4, New York

REFERENCES

1. Cleare, H. M., Splettstosser, H. R., and Seemann, H. E. Experimental study of mottle produced by x-ray intensifying screens. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *88*, 168–174.
2. Rossmann, K. Modulation transfer function of radiographic systems using fluorescent screens. *J. Opt. Soc. Am.*, 1962, *52*, 774–777.
3. Rossmann, K. Recording of x-ray quantum fluctuations in radiographs. *J. Opt. Soc. Am.*, 1962, *52*, 1162–1164.
4. Rossmann, K. Image-forming quality of radiographic screen-film systems: line spread-function. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1963, *90*, 178–183.
5. Sturm, R. E., and Morgan, R. H. Screen intensification systems and their limitations. Am. J. Roentgenol. & Rad. Therapy, 1949, *62*, 617–634.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

Editor: TRAIAN LEUCUTIA, M.D.
Assistant to the Editor: KENNETH L. KRABBENHOFT, M.D.
Associate Editors: HARRY HAUSER, M.D., RUSSELL H. MORGAN, M.D., EDWARD B. D. NEUHAUSER, M.D., WENDELL G. SCOTT, M.D.
Consulting Editorial Board: See front cover.
Published by: CHARLES C THOMAS, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois.

Issued monthly. Annual subscription: United States, Mexico, Cuba, Central and South America, and Canada $15.00; other countries, $17.00. Current single numbers, $1.50. Advertising rates submitted on application. Editorial office, 110 Professional Building, Detroit 1, Michigan. Office of publication, 301–327 East Lawrence Avenue, Springfield, Illinois. Information of interest to authors and readers will be found on page ii.

AMERICAN ROENTGEN RAY SOCIETY

President: E. E. Barth, Chicago, Ill.; *President-Elect:* R. M. Caulk, Washington, D. C.; *1st Vice-President:* A. C. Singleton, Toronto, Ont., Canada; *2nd Vice-President:* G. Cooper, Jr., Charlottesville, Va.; *Secretary:* C. A. Good, Mayo Clinic, Rochester, Minn.; *Treasurer:* S. W. Brown, 1467 Harper Street, Augusta, Ga.

Executive Council: E. E. Barth, R. M. Caulk, A. C. Singleton, C. A. Good, S. W. Brown, W. Bailey, J. F. Roach, L. E. Etter, T. Leucutia, H. G. Reineke, H. O. Peterson, J. C. Cook, J. D. Reeves, H. M. Stauffer, T. F. Leigh, E. L. Pirkey, J. P. Medelman, Chairman, 110 Birchwood Avenue, Birchwood, White Bear Lake 10, Minn.

Program Committee: C. A. Good, Rochester, Minn.; J. F. Roach, Albany, N. Y.; T. Leucutia, Detroit, Mich; L. E. Etter, Pittsburgh, Pa.; J. P. Medelman, White Bear Lake, Minn.; H. O. Peterson, Minneapolis, Minn.; R. M. Caulk, Chairman, Washington, D. C.

Publication Committee: M. M. Figley, Seattle, Wash.; R. N. Cooley, Galveston, Tex; J. F. Holt, Ann Arbor, Mich.; B. R. Young, Philadelphia, Pa.; J. F. Roach, Chairman, Albany, N. Y.

Finance and Budget Committee: T. F. Leigh, Atlanta, Ga.; E. L. Pirkey, Louisville, Ky.; C. B. Holman, Rochester, Minn.; J. A. Campbell, Indianapolis, Ind.; W. Bailey, Chairman, Los Angeles, Calif.

Committee on Scientific Exhibits: R. R. Greening, Philadelphia, Pa.; J. S. Dunbar, Montreal, Que., Canada; L. E. Etter, Chairman, Pittsburgh, Pa.

Representatives on the American Board of Radiology: C. A. Stevenson, Spokane, Wash.; J. F. Roach, Albany, N. Y.; C. A. Good, Rochester, Minn.

Director of Instructional Courses: H. O. Peterson, Minneapolis, Minn.; *Manager of the Annual Meeting:* J. C. Cook, 110 Professional Building, Detroit 1, Mich.

Editor: T. Leucutia, 110 Professional Building, Detroit 1, Mich.

Sixty-fourth Annual Meeting: Queen Elizabeth Hotel, Montreal, Quebec, Canada, October 8–11, 1963.

AMERICAN RADIUM SOCIETY

President: Charles G. Stetson, Tenafly, N. J.; *President-Elect:* Joseph H. Farrow, New York, N. Y.; *1st Vice-President:* Juan A. del Regato, Colorado Springs, Colo.; *2nd Vice-President:* John L. Pool, New York, N. Y.; *Secretary:* Justin J. Stein, Los Angeles, Calif.; *Treasurer:* Milton Friedman, 1016 Fifth Ave, New York 28, N. Y.

Executive Committee: Jesshill Love, Chairman; Robert L. Brown; Gilbert H. Fletcher; Charles G. Stetson; Justin J. Stein; Joseph H. Farrow; Juan A. del Regato; John L. Pool; Milton Friedman.

Scientific Program Committee: Charles G. Stetson, Chairman; A. N. Arneson, St. Louis, Mo.; Milton Friedman, New York, N. Y.; Harold E. Johns, Toronto, Ont.; Henry S. Kaplan, Palo Alto, Calif.; Calvin T. Klopp, Washington, D. C.; Milford D. Schulz, Boston, Mass.; Joseph H. Farrow, Ex officio.

Committee on Arrangements: Henri LeClaire, Chairman, Cincinnati, Ohio; Manuel Garcia, Chairman Designate, New Orleans, La.; Albert L. Allen, Huntington, W. Va.; Robert D. Berkebile, Elyria Ohio; H. Peter Mueller, Belmont, Mass.; Ralph M. Scott, Louisville, Ky.; Milton Friedman, Ex officio.

Publication Committee: Harry Hauser, Chairman, Cleveland, Ohio; Wendell C. Hall, Hartford, Conn.; Martin Van Herik, Rochester, Minn.

Public Relations Committee: H. Peter Mueller, Chairman, Belmont, Mass.; Harold W. Jacox, New York, N. Y.; Charles H. Peterson, Roanoke, Va.

Janeway Lecture Committee: Edith H. Quimby, Chairman, New York, N. Y.; William S. MacComb, Houston, Tex.; Clifford L. Ash, Toronto, Ont.

Representatives on the American Board of Radiology: Frederick W. O'Brien, Boston, Mass.; Bernard P. Widmann, Philadelphia, Pa.; Donald S. Childs, Jr., Rochester, Minn.

Representatives on the National Committee on Radiation Protection: Robert Robbins, Philadelphia, Pa.; Herbert M. Parker, Richland, Wash.

Representative on the Board of Chancellors of the American College of Radiology: Milford D. Schulz.

Forty-sixth Annual Meeting: Greenbrier Hotel, White Sulphur Springs, W. Va., April 13–16, 1964.

EDITORIALS

SOME ASPECTS OF TELEVISION RADIOLOGY

IN 1951, Morgan and Sturm were directly televising the fluorescent screen by image orthicon camera and Janker in 1958, was doing similarly. The use of image intensification coupled with the television camera or with moving picture cameras has made possible bold new advances in diagnostic radiography. Various image intensifiers, television cameras and recording cameras are now available.

Duckett[1] commented editorially in this JOURNAL in 1960 on the use of telefluoroscopy at Hôpital Jean-Talon and Hôtel-Dieu de Montréal. He pointed out the advantages of daylight telefluoroscopy, dispensing with the need for adaptation and dark room working. It has enabled most examinations to be performed remotely and viewed in another area. The use of closed-circuit television provides rapid consultation and film data comparison between the two hospitals. This is an aspect which they have put to excellent use and consider it a very important part of their present facilities.

In the field of gastrointestinal work, the use of image intensification increased the fluoroscopist's appreciation of the anatomy under consideration, and can yield a higher degree of immediate information. At the same time the exposure to ionizing radiation is decreased both to the patient and to the physician. In colon examinations image intensification is of unquestionable value. In upper gastrointestinal studies, the present equipment may seem somewhat bulky unless operated remotely or with power assistance. This really is a rather small inconvenience when weighed against the positive factors. The attachment of a television monitor to the image intensification unit enables many observers to view the examination while it is in progress, making it both an excellent teaching aid as well as providing the possibility of instantaneous consultation during the study.

In cardiovascular work cinematography coupled with image intensification provides a film record which can be re-examined again and again in moving sequence, letting the eye find the small imperfections which might otherwise be missed with a timed radiographic procedure. This method has now become an indispensable part of the clinical diagnostic investigations, enhancing the extremely rapid progress which has been made in surgery of the heart and great vessels during the last few years.

Combined cinematography and image intensification may also be used with considerable success in urology for recording certain functions or dysfunctions of portions of the genitourinary tract. A good example of this aspect is given by Tristan and his associates[2] who use a combined synchronous and simultaneous cinecystourethrography and direct cystometry for evaluation of the normal and pathologic physiology of the bladder outlet. These authors fill the bladder under light general anesthesia with opaque material and when the bladder is palpable above the symphysis pubis, they make a percutaneous extraperitoneal puncture and insert a polyethylene tubing which is connected to a PR 23-2D-300 Statham transducer. Intravesical pressure recordings are made using a seven channel Electronics for Medicine oscilloscopic photographic recorder. The pressure within the bladder is continuously observed on the oscilloscope and a simultaneous photographic recording is made with either a 16 mm. or a 35 mm. motion picture camera which is mounted on the image intensifier. The whole procedure can be carried out in daylight and is television monitored.

---

[1] Duckett, G. Daylight telefluoroscopy. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1960, *84*, 566-567.

[2] Tristan, T. A., Murphy, J. J., Schoenberg, H. W., Toborowsky, R., and Epperson, R. D. Cinefluorographic investigation of genitourinary tract function; bladder neck dysfunction. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1963, *90*, 1-14.

Recently, Matsuda and his colleagues[3] gave an excellent account of the possible uses of an improved remote control x-ray television system, in which the image amplification is done by a 9 inch vidicon intensifier and the unit is adjustable to various procedures for telefluoroscopy, telecineroentgenography and telefluororoentgenography. The patient is examined remotely on a table which has longitudinal sliding, lateral traverse and up and down tilting. The amplified image as well as the general view of the examination room are transmitted not only to the control room but to other specially equipped parts of the hospital. A triangular mark is inscribed electrically for pointing out the lesion to observers in the other rooms and this mark can also be recorded on a spot film or a cine film. Since 1961, Matsuda and his colleagues have used this improved x-ray television system instead of conventional roentgenography in all instances of intravenous pyelography, myelography, venography including splenoportography, and bronchography. They have also used it in one-third of the gastrointestinal cases and expect that all studies will be performed in this fashion with the acquisition of more equipment.

A very intriguing aspect in television radiology is the possible application of color television. Fisher and Gershon-Cohen[4] in 1958 described a television technique for contrast enhancement and color translation of roentgenograms. Using a closed-circuit television system with a flying spot cathode-ray tube scanner, the information on the roentgenograms is converted to a television video signal. By means of electronics it is possible to clip the video signals at various lambert levels and the signals of interest can thus be enhanced. Normally, the eye can just barely discern a brightness level difference of 2 per cent. With this system it is possible to increase the difference to 20 per cent, and areas side by side on a roentgenogram with only the 2 per cent difference in brightness would be much more easily perceptible. In addition to mere enhancement in monochrome display, the use of a color converter and a color monitor to enhance contrast has added value. The use of both the monochrome and color contrast enhancement is desirable in many cases.

In 1959, Gershon-Cohen and Fisher[5] pointed out the advantages of monochrome contrast enhancement in scanning routine roentgenograms. By varying the contrast of the television monitor in viewing a single film, the same information can be garnered that would ordinarily require several films exposed by varying techniques. The advantage here, of course, is in being able to obtain all of the information from a single roentgenogram in an examination that would usually necessitate several roentgenograms, thus reducing patient exposure considerably.

Of even greater promise appears to be the use of monochrome and color television enhancement in the interpretation of radioisotopic photoscans. Charkes and Gershon-Cohen studied this aspect and in their latest report[6] beautifully demonstrated the value of the procedure. The method, which is similar to that formerly described in using closed-circuit television system with a flying spot cathode-ray tube scanner on roentgenograms, allows presentation of low visual contrast data not previously obtainable. Areas which to the human eye on the preliminary photoscan show only poor degrees of contrast are enhanced and through the use of color are much more easily detected than by means of the original photoscans. The possibilities for scanning brain, liver, thyroid, bone and other denser organs will be of great importance in enabling the physician to pick up small foci which formerly were difficult to identify.

---

[3] Matsuda, H., Nagaoka, T., Nakahori, T., Takai, G., Sohma, J., Nakai, A., and Ninomiya, K. X-ray examination with an improved x-ray television unit. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1963, *89*, 432–442.

[4] Fisher, J. F., and Gershon-Cohen, J. Television technique for contrast enhancement and color translation of roentgenograms. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1958, *79*, 342–347.

[5] Gershon-Cohen, J., and Fisher, J. F. Television contrast expansions of single roentgenograms. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *81*, 325–327.

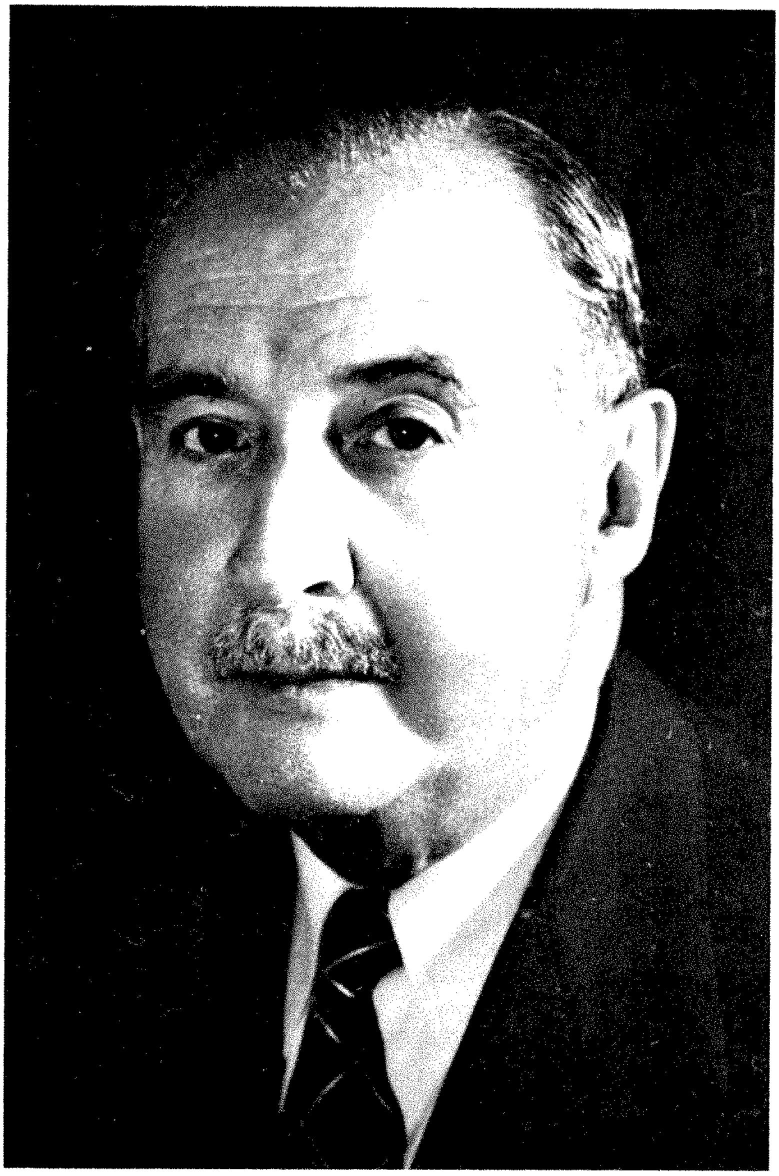
[6] Charkes, N. D., and Gershon-Cohen, J. Color television contrast expansion of photoscans. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1963, *90*, 406–409.

One could enumerate other aspects of possible future development. Clearly, the uses of image intensification coupled with television, both as a monitor and as a scanning device, for enhancement in monochrome and color display, and the use of cineradiography are limited only by the bounds of appreciation of their applicability and the scope of the ever-broadening achievements on a rapidly advancing technical front.

George A. Kling, M.D.

Harper Hospital
Detroit 1, Michigan

* * *



MANUEL F. MADRAZO

1890-1963

DR. MANUEL F. MADRAZO, a pioneer of Orthopedics and Radiology in Mexico, was born in Leon, State of Guanajuato in Mexico on November 12, 1890. He studied in his native city through high school and then at the School of Medicine of the National University of Mexico.

In 1913 upon the recommendation of the University, he became associated with Dr. Noguchi in work dealing with the cultivation of Koch's bacillus and with Drs. Swift and Ellis in tuberculin reaction studies. He then went to Switzerland where he served on the visiting staff of Dr. Rollier in Leysin.

In 1916 Dr. Madrazo returned to Mexico, was graduated in 1918 and was married the same year to Miss Laura Garamendi. He and his wife went to New York where he served as resident in the Hospital for Bone and Joint Diseases under Dr. H. Finkelstein and then to Colonia, New Jersey, to the Reconstruction Hospital under Dr. Fred H. Albee.

Upon his return to Mexico, he was appointed Adjunct Professor of Biological Chemistry, later Chief of Surgical Clinics and then Professor. He is credited in an article written by Dr. Juan Farill of Mexico and published in the American Edition of the *Journal of Bone and Joint Surgery* in having brought to Mexico the first Albee electric saw and two orthopedic tables. He performed the first spinal fusion in Mexico for Pott's disease and is considered as having been the first orthopedic surgeon with specialized training.

Dr. Madrazo carried on his own private radiologic work. When a leading medical radiologist of the capital retired, physicians began sending patients to him for radiologic consultation. In this manner his diagnostic work grew steadily. His frequent visits to the United States and his close contact with Dr. James T. Case at Northwestern University further stimulated his interest and added to his knowledge of radiology, so much so that he abandoned his orthopedic practice to devote his time exclusively to radiology, both diagnostic and therapeutic. He soon became consultant to the most capable physicians and surgeons in Mexico City.

He was elected to occupy the Chair of Radiology at the National Academy of Medicine, became a Corresponding Member of the American Roentgen Ray Society in 1928, was elected an Honorary Fellow of the American College of Radiology in 1930, was a Member of the Radiological Society of North America since 1931, third Vice-President in 1939 and its Counsellor in Mexico until his death. Dr. Madrazo was also a Member of the Academy of Surgery of Mexico, and was made Emeritus Member upon retirement because of illness in 1959. He was a Founder and Past President of the Sociedad Mexicana de Radiología and held honorary memberships in the Radiological Societies of Argentine, Colombia, Cuba, Italy, Panama, Ecuador, and Peru. He was a Member of the Sociedad Mexicana de Cancerología and several other Mexican Societies, represented his Country at the Fifth Latin American Congress of Surgeons in Dallas in 1933, at the Fifth International Congress of Radiology in Chicago in 1937, and at the Sixth International Congress of Radiology in London in 1950.

In 1952 Dr. Madrazo was elected President of the Fourth Inter-American Congress of Radiology and in 1956 President of the Eighth International Congress of Radiology. The Government of France honored him with the Decoration of Officer of the Academy and of Public Instruction; the Government of Colombia with the Cruz de Boyacá. He was a recipient of the Gold Medal of the Inter-American College of Radiology and the Centre Antoine Béclère.

Affable and honorable, a true gentleman, Dr. Madrazo was a leader by his mere presence, a man who had the right to the title of Marqués del Valle de la Colina from his paternal grandfather, a title which he never validated but which made Dr. Juan A. del Regato exclaim in homage to Mexican Radiology in 1956, during the Convocation of the American College of Radiology: " . . . to the gentleman of unique elegance and nobility who disdains the title but who incarnates the dignity of the title itself." Upon the diploma given to him on that occasion, it was written: "he has contributed greatly to human knowledge and has well served his profession, his country and mankind."

Dr. Manual F. Madrazo died in Mexico City on March 21, 1963.

Guillermo Santín, M.D.

EVERETT L. PIRKEY

1915-1963

THE death of Everett L. Pirkey ended a brilliant and distinguished career as a teacher of residents and medical students and of service to patients. He died on July 30, 1963, as a result of a brain lesion from which he had suffered for the past 3 years.

Dr. Pirkey's entrance into the specialty of Radiology was one of chance. After graduating from medical school, he decided to become an orthopedic surgeon. This career was early and abruptly terminated when he was called to active duty in the Army, January 13, 1941, and served his country for 5 years.

Dr. Pirkey was born in Louisville, Kentucky, on January 17, 1915. He received the degrees of Bachelor of Science (1935) and Doctor of Medicine (1939) from the University of Louisville. After an internship at Butterworth Hospital, Grand Rapids, Michigan, he began his residency in orthopedics at Louisville General Hospital. On entrance to active duty at Fort Knox, he was assigned to the Mumps Ward. It was at this time that he became interested in Radiology. He not only got himself assigned to the X-ray Department, but within a year or so was made Chief of that Department. He served 3 years in England and in Europe as Chief of Radiology in various Army hospitals, returned to the United States, was discharged with the rank of Lieutenant Colonel, and finished his radiologic training at St. Luke's Hospital in Chicago. He joined our faculty in 1946. He was the first full-time radiologist at Louisville General Hospital, and was made Professor and Chairman of the Department in 1952.

The contributions of Dr. Pirkey to medical science are numerous and particularly related to roentgenologic diagnosis. His major research interests were early diagnosis of gastric tumors with the balloon technique, color roentgenograms for teaching medical students and contrast media for gastrointestinal studies. Over 25 of his articles have been published.

Despite his primary devotion to the teaching and practice of Radiology, he became interested in the medical education as a whole. He clearly understood that, with the explosively rapid advancing knowledge in medical science, the old curriculums were no longer adequate to prepare students to deal with this vast information. He decided to correct the situation and requested and got a 6 month leave of absence in 1958 to direct the curriculum-revision project. However, when the nature of his illness became known, he resigned as Chairman of the Department of Radiology and became full-time Director of the curriculum project. A large grant was obtained from the Commonwealth Foundation to carry out his study. This has now resulted in the new and radically changed curriculum which goes into effect with the freshman class this fall.

Everett Pirkey belonged to varied organizations, both local and national. He held office in many of them at one time or another. He served as President of the Kentucky State Radiological Society, was a member of the Board of Directors of the Kentucky Chapter of the American Cancer Society, Chairman of the Scientific Exhibit Committees of Radiological Society of North America and the Kentucky State Medical Association. He was appointed to the Kentucky Governor's Advisory Committee on Atomic Energy. He was also active in college affairs and served on its Committee on Education. At the time of his death, he was a member of the Executive Council of the American Roentgen Ray Society.

Dr. Pirkey is survived by his devoted wife, the former Evelyn Boone, and their daughter, Diane Pirkey of Washington, D. C.

Everett's wise counsel and genial good fellowship will be greatly missed by his many friends and associates.

J. T. Ling, M.D.

PETER E. RUSSO

1904-1963

DEATH came quickly to Dr. Peter E. Russo on March 13, 1963, in Oklahoma City, from acute coronary thrombosis.

Dr. Russo was born in Italy but came to the United States at 8 years of age. His early education was obtained in Cleveland, Ohio, at public and parochial schools; he was a graduate of Western Reserve University in 1926 and St. Louis University School of Medicine in 1930. Following internship in St. John's Hospital of Cleveland, he practiced general medicine in that city for 10 years. In 1941, he accepted a residency in radiology at the University Hospitals in Oklahoma City, was appointed

Clinical Professor of Radiology at the University of Oklahoma School of Medicine in 1952 and Professor of Radiology in 1956; he served as Chairman of the Department of Radiology from 1949–1957. From 1943 to 1947 he was associated in the private practice of radiology with the late Dr. John Heatley. He opened his own office in 1947, and in 1949 was founder of a radiology partnership which finally numbered 5 members, engaging in office and hospital practice in Oklahoma City.

Dr. Russo was a Fellow of the American College of Radiology, and a member of the American Roentgen Ray Society, the American Radium Society, and of the Radiological Society of North America, serving as vice-president of the latter in 1956. He was President of the Oklahoma Radiological Society in 1948 and 1949, President of the Southwestern Chapter of the American Society of Nuclear Medicine in 1959 and 1960, and President of the Rocky Mountain Radiological Society in 1961. At the time of his death he was President-Elect of the Oklahoma State Medical Association and was to assume the office of President in May, 1963.

Pete Russo was a well rounded person with many interests and accomplishments but primarily the field of Medicine and particularily Radiology drew his greatest attention. Medicine gained from his efforts. He contributed 33 papers to the radiologic literature and for many years was a distinguished member of the Department of Abstracts of the AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE. Medical students and residents were helped immeasurably from his store of scientific knowledge and warm personality. He played a good game of golf and made a "hole in one," on two occasions. An accomplished artist, he was especially proud of receiving the first prize at the Amateur Art Show for Professional and Business Men for his portrait of his daughter Petrina. Pete is deeply missed by his many friends, both in and outside Medicine.

Dr. Russo is survived by his wife, Magdalene Agnes, and 4 children Odilia, Petrina and Peter, in Oklahoma City, and Mrs. Don Horton of Alberta, Canada.

BERT E. MULVEY, M.D.

NEWS ITEMS

FACULTY OF RADIOLOGISTS, ROYAL COLLEGE OF SURGEONS IN IRELAND

At the Royal College of Surgeons in Ireland, on Friday, June 21, 1963, the President of the Royal College of Surgeons in Ireland, Mr. T. Millin, F.R.C.S.I., conferred the Fellowship of the Faculty of Radiologists on 20 doctors.

On Saturday, June 22, 1963, Dr. Ross Golden, M.D., F.F.R., R.C.S.I., Hon., gave an illustrated lecture on "The Gross Growth of Carcinoma of the Stomach."

The second Annual Dinner of the Faculty of Radiologists was held in the College Hall on the evening of Saturday, June 22, 1963. The guests included the two Honorary Fellows, Dr. Ross Golden, Los Angeles, and Dr. Leo Henry Garland, San Francisco, on whom the Honorary Fellowship of the Faculty of Radiologists, Royal College of Surgeons in Ireland had just been conferred by the President of the Royal College of Surgeons in Ireland.

The Dean of the Faculty of Radiologists, Mr. D. J. Riordan, F.R.C.S.I., F.F.R.R.C.S.I., during his address welcomed all new Fellows and guests.

ELEVENTH INTERNATIONAL CONGRESS OF RADIOLOGY

The Eleventh International Congress of Radiology will be held September 22–28, 1965 in Rome, Italy, and will be presided over by Prof. Luigi Turano, Director of the Radiological Institute of the University of Rome.

The scientific program of the Congress will include topics on diagnostic radiology, therapeutic radiology, nuclear medicine, radiobiology and radiologic physics. A preliminary plan will be sent, during the first months of 1964, to the National Societies of Radiology which have already participated in previous Congresses and to other Societies upon request.

Technical, industrial and scientific exhibitions will form an important part of the meeting and attractive social functions will be arranged.

For further information write to the General Secretary, Prof. Dr. Arduino Ratti, Via Moscova, 44/1, Milano, Italy.

FIRST INTERNATIONAL RESEARCH CONFERENCE IN ORAL ROENTGENOLOGY

The First International Research Conference in Oral Roentgenology will be held November 21–23, 1963, at the Nebraska Center for Continuing Education in Lincoln, Nebraska.

The Conference will provide a high-level exchange of technical and professional information. Papers will be presented on research in diagnosis, x-ray equipment, radiation protection, isotopes and nuclear particles, and radiobiology. Sources of research support and potentials of radiologic research will also be discussed.

Representatives from dental and medical schools, research institutes, and industries are expected to attend.

The Conference is sponsored by the American Academy of Oral Roentgenology and supported by the National Institute of Dental Research and the Fund for Dental Education.

Requests for further information should be addressed to Dr. Clifton E. Crandell, University of North Carolina School of Dentistry, Chapel Hill, N. C.

SYMPOSIUM ON BIOLOGICAL EFFECTS OF NEUTRON IRRADIATIONS

The first scientific symposium sponsored by the International Atomic Energy Agency in the United States will be held at Brookhaven National Laboratory, Upton, Long Island, October 7–11, 1963, in cooperation with the Laboratory and with the U. S. Atomic Energy Commission. The subject of the symposium is the biological effects of neutron irradiations.

This symposium is intended to provide an opportunity for scientists to discuss the experimental information available at present on the biological action of neutrons and to evaluate future perspectives. It is expected that the question of relative biological effectiveness will be extensively discussed, in view of the importance this factor has for the formulation of adequate health and safety regulations. It is further expected that laboratory experience related to practical applications of neutron radiation, such as in radiation treatment or plant breeding, will be considered.

It is also planned to reserve one session for a general discussion of the practical implications of the fundamental work on neutron irradiation effects discussed in other sessions. The use of neutron irradiation in medicine and in agriculture, respectively, will be the main topics.

For further information please write to International Atomic Energy Agency, Room 2265, United Nations Building, New York City, N.Y.

POST-GRADUATE MEETING IN RADIOLOGY

The annual Post-Graduate Meeting in Radiology will be held at the University of Kansas Medical Center on February 17th, 18th, and 19th, 1964. The program includes 8 guest speakers, prominent in the field of Radiology throughout the United States and Canada.

For further information please write to Dr. G. M. Tice, Department of Radiology, University of Kansas Medical Center, Rainbow Boulevard at 39th Street, Kansas City 3, Kansas.

UNIVERSITY OF MINNESOTA CONTINUATION COURSE IN RADIOLOGY

The University of Minnesota announces a Continuation Course in Neuroradiology, to be held November 4–8, 1963.

In this course, pertinent fundamental aspects of the subject will be reviewed briefly and important advances in basic knowledge, diagnosis and treatment will be discussed. Clinical considerations will also be stressed.

For further information contact Center for Continuation Study, General Extension Division, Minneapolis, Minnesota, 55455.

ADVANCED STUDY AND RESEARCH IN RADIOLOGY

The Donner Laboratory, University of California, announces an opportunity for advanced study and research in radiology. Activities include investigation of the biological effects of high-energy particles and participation in clinical radiological projects utilizing high-energy particles.

One or two courses in the graduate program in biophysics and medical physics may be taken concurrently.

Applicants must have completed residency in radiology or comparable training. Stipend will depend on qualifications and experience.

Application forms are available from: John H. Lawrence, M.D., Director, Donner Laboratory, University of California, Berkeley, California, 94720.

LECTURES ON X-RAY DIAGNOSIS OF BONE LESIONS IN MEXICO CITY

The X-Ray Department of the Mexico City General Hospital has arranged a series of lectures on "X-Ray Diagnosis of Bone Lesions" to be given by Dr. Harold G. Jacobson of New York City, December 5–7, 1963.

The organizers invite all radiologists who might be interested to attend these lectures and at the same time visit Mexico.

Further information may be obtained from: Dr. Jorge Ceballos-Labat, Chairman of the X-Ray Department, Hospital General Dr. Balmis #148, México 7, D. F., México.

BOOK REVIEW

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

UNIT-STEP RADIOGRAPHY; SIMPLIFICATION OF MEDICAL RADIOGRAPHY THROUGH MANUAL AND AUTOMATIC USE OF AN EXPOSURE VALUE SCALE (XVS) SYSTEM AND STANDARDIZATION. By Gerhart S. Schwarz, M. D., Department of Radiology, College of Physicians and Surgeons, Columbia University, Radiological Service, Presbyterian Hospital, New York, New York. Cloth. Price, $8.75. Pp. 230, with 33 illustrations. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1961.

One definition of progress is to move forward, and in no field of medicine has the technical advance in equipment been as rapid as in radiology. Yet, even with the development of high kilovoltage tubes, image intensification, three phase transformers, and automatic film processing, the Technique Chart with fixed kilovoltage, milliamperage, and time settings remains beside the modern equipment transfixed to the wall like a beacon from the past.

The author admirably describes a unit step system for manual and automatic use which in essence could remove the outdated Technique Chart from the wall and would lead to a more rapid handling of patient roentgenography by reducing the human error. Unit step roentgenography or the XVS system is similar to the EVS (Exposure Value Scale) system of photography. Each unit increase doubles the roentgenographic effect on the film.

In the manually used form, unit index numbers or half unit numbers are assigned to the kilovoltage, milliamperage, and time controls of the roentgenographic console. A caliper has been devised which reads directly in unit steps or half steps of the measured part. The technician simply measures the part to be roentgenographed, sets the controls (kilovoltage, milliamperage, and time) in terms of index numbers which equal the value read off the caliper scale and activates the switch.

The manual system is applicable to special areas such as high kilovoltage gastrointestinal roentgenography, extremity roentgenography using cardboard holders, and conventional chest and spine roentgenography. It can easily be altered for various grid ratios, tube distances, and filters as well as for Par Speed and High Speed screens.

The author devotes considerable attention to the definition of the unit steps for kilovoltage, milliamperage and time, and to the proper labeling of the control console. He discusses the development of the measuring caliper and analyzes the possible human technical errors.

The unit step system can also be utilized as a means to automation; in this respect manufacturers have recently made notable headway, producing at least one fully automatic equipment and many others which are partially automatic. In nearly all departments photo-timing for spot roentgenography has become a necessity. Many large departments which have developed special procedures for roentgenographic study as, for instance, of the gastrointestinal tract, nervous system, and chest are utilizing three phase equipment with automatic exposure control, resulting within certain limits in a uniform and reproducible technique.

The reviewer readily agrees with the author that the system will benefit individual departments and that it will prove even more useful if applied to larger areas. A unit system of this type may in the future be employed on a national scale in an attempt to produce a standardized medical roentgenographic technique system similar to that now in operation in photography.

The book is highly recommended to radiologists, technicians and equipment manufacturers who share equally in this problem.

ROBERT L. WILLIS, M.D.

BOOKS RECEIVED

BROKEN LONG BONE: ITS BIONOMICS AND MAN. By Robert T. McElvenny, M.D., Senior Attending Surgeon, Chicago Wesley Memorial Hospital, Chicago, Ill.; with illustrations and additions by Ned Murray Grove, M.D., Department of Orthopaedic Surgery, Northwestern University Medical School, Chicago, Ill. Cloth. Pp. 292, with some illustrations. Price, $11.50. Charles C Thomas, Publisher, 301–327 East Lawrence Ave., Springfield, Ill., 1963.

The Role of Magnesium in Biologic Processes. By Jerry K. Aikawa, M.D., Associate Professor of Medicine, University of Colorado School of Medicine, Denver, Colo. Cloth. Pp. 118. Price, $6.75. Charles C Thomas, Publisher, 301–327 East Lawrence Ave., Springfield, Ill., 1963.

Cancer of the Female Reproductive Organs. By Alfred I. Sherman, M.D., Associate Professor of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, Mo.; Director of the Gyncological Cancer Service at Washington University and Barnes Hospital Clinics, St. Louis, Mo.; Consultant in Gynecology to the Mallinckrodt Institute of Radiology, St. Louis, Mo.; Associate Obstetrician and Gynecologist to Barnes Hospital, St. Louis Children's Hospital, and Allied Hospitals, St. Louis, Mo.; Consultant and Visiting Physician to City Hospital, Homer G. Phillips Hospital, St. Luke's Hospital, and Jewish Hospital, St. Louis, Mo.; Diplomate, American Board of Obstetrics and Gynecology. Cloth. Pp. 338, with many illustrations. Price, $13.75. The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, Mo., 1963.

Annual Review of Medicine. Volume 14. Edited by Arthur C. Degraff, M.D., New York University College of Medicine; Associate editor, William P. Creger, M.D., Stanford University School of Medicine. Cloth. Pp. 468, with some illustrations. Price, $8.50. Annual Reviews, Inc., 231 Grant Ave., Palo Alto, Calif., 1963.

Orthopedic Diseases: Physiology, Pathology, Radiology. Second edition. By Ernest Aegerter, M.D., Professor of Pathology and Director of the Department of Pathology, Temple University Medical Center and School of Medicine; Professor of Orthopedic Pathology, University of Pennsylvania Graduate School of Medicine; Chief in Pathology, Philadelphia General Hospital; Consultant in Pathology, Frankford Hospital, United States Naval Hospital, Veterans Administration Hospital, Shriners Hospital for Crippled Children, Philadelphia; Pennsylvania State Hospital for Crippled Children, Elizabethtown, Pa.; the A. I. duPont Institute, Wilmington, Del.; and John A. Kirkpatrick, Jr., M.D., Radiologist, St. Christopher's Hospital for Children; Associate Professor of Radiology (Pediatrics), Temple University School of Medicine; Radiologist, Children's Heart Hospital; Attending (Radiology), Veterans Administration Hospital, Philadelphia. Cloth. Pp. 786, with many illustrations. Price, $16.00. W. B. Saunders Company, Philadelphia, Pa., 1963.

Hermodsson's Roentgenological Studies of Traumatic and Recurrent Anterior and Inferior Dislocations of the Shoulder Joint. Edited by H. F. Moseley, M.A., D.M., M.Ch. (Oxon.), F.R.C.S. (Eng. and Canada), F.A.C.S., Director, Accident Service, and Surgeon, Royal Victoria Hospital; Associate Professor of Surgery, McGill University, Montreal; Hunterian Professor, Royal College of Surgeons of England; and B. Övergaard, M.L., Merck, Sharp and Dohme Research Fellow; Accident Service, Royal Victoria Hospital, Montreal. Cloth. Pp. 167, with many illustrations. Price, $8.00. McGill University Press, 3458 Redpath St., Montreal 25, Quebec, Canada, 1963.

Gamma-Rays of Radionuclides in Order of Increasing Energy. By D. N. Slater, Department of Chemistry, Brunel College of Technology, London. Cloth. Pp. 209. Price, $9.00. Butterworth Inc., 7235 Wisconsin Avenue, Washington 14, D. C., 1962.

Diseases of the Adrenal Glands: Radiologic Diagnosis; with emphasis on the use of presacral retroperitoneal pneumography. By Morton A. Meyers, M.D., Department of Radiology, Presbyterian Hospital, Columbia-Presbyterian Medical Center, New York. Cloth. Pp. 98, with many illustrations. Price, $5.75. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1963.

The Radiologic Clinics of North America: Symposium on Diagnostic Roentgenology of the Chest. Volume I. Guest Editor, Benjamin Felson, M.D. Cloth. Pp. 456, with many illustrations. W. B. Saunders Company, West Washington Square, Philadelphia 5, Pa., 1963.

Diseases of the Chest. Second edition. By H. Corwin Hinshaw, M.D., Ph.D., D.Sc., Clinical Professor of Medicine, University of California School of Medicine, San Franciso; and L. Henry Garland, M.B., B.Ch., M.D., Clinical Professor of Radiology, University of California School of Medicine, San Francisco. Cloth. Pp. 798, with 743 illustrations. Price, $20.00. W. B. Saunders Company, West Washington Square, Philadelphia 5, Pa., 1963.

The Cytologic Diagnosis of Cancer. Second edition. By Ruth M. Graham, Roswell Park Memorial Institute, Buffalo, New York. Cloth. Pp. 387, with many illustrations. Price, $14.00. W. B. Saunders Company, West Washington Square, Philadelphia 5, Pa., 1963.

Medical Electronics in Cardiovascular Disease. Edited by Charles K. Friedberg, M.D., Assistant editor, Ephraim Donoso, M.D. Cloth. Pp. 274, with some illustrations. Price, $10.00. Grune & Stratton, Inc., 381 Park Avenue South, New York 16, N. Y., 1963.

ABSTRACTS OF RADIOLOGICAL LITERATURE

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Neck and Chest

Schmidt, H. W. *et al.:* Pulmonary changes seen in lung purpura and some of the other collagen diseases 885
Pugsley, H. E., Brown, A. S., and Cheung, O. T.: Chronic cavitary histoplasmosis of the lung 885
Borrie, J.: Fifty thoracic hydatid cysts 885
Davis, S., Gardner, F., and Qvist, G.: The shape of a pleural effusion 886
Williams, B. *et al.:* Patent ductus arteriosus and osteoarthropathy 886
Sanger, P. W., Taylor, F. H., and Robicsek, F.: Deformities of the anterior wall of the chest 886
Meagher, R. P., Lupien, J., and Albert, S. N.: Postoperative rupture of the esophagus 887

Abdomen

Texter, E. C., Jr. *et al.:* Criteria for the diagnosis of hiatal hernia 887
Groves, L. K., and Effler, D. B.: Cancer of the gastric cardia associated with esophageal hiatus hernia 888
Mathieson, A. J. M.: The Billroth-I recurrent ulcer 888
Riordan, A. F., Bergmann, K., and Leslie, E. V.: Bowel preparation for radiologic examination: comparison of techniques 888
Flemma, R. J. *et al.:* Percutaneous transhepatic cholangiography in the differential diagnosis of jaundice 889
Arcomano, J. P., Heroy, W. W., and Barnett, J. C.: Fixed filling defects of the gallbladder 890
Pitman, R. G., and Davies, A.: The clinical and radiological features of spontaneous internal biliary fistulae 890

ROENTGEN DIAGNOSIS

NECK AND CHEST

SCHMIDT, HERBERT W., HARGRAVES, MALCOLM M., ANDERSEN, HOWARD A., and DAUGHERTY, GUY W. Pulmonary changes seen in lung purpura and some of the other collagen diseases. *Canad. M. A. J.*, Mar. 30, 1963, *88*, 658–665. (From: Section of Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minn.)

The roentgenographic findings in some of the collagen diseases as well as a brief discussion of the etiologic factors are presented.

Pulmonary purpura or necrotizing alveolitis usually begins with hemoptysis, occasionally associated with cough and weakness. The roentgenographic changes are the result of intrapulmonary hemorrhage. Typically, there is a diffuse infiltrate having a butterfly wing appearance. The infiltrate may clear spontaneously but often recurs. Renal biopsy frequently shows glomerulonephritis. The authors have observed similar pulmonary changes in patients with glomerulonephritis clinically.

Pulmonary hemorrhage with identical roentgenographic changes also occurs in periarteritis nodosa but in addition thrombosis of the arteries may be noted. The latter may lead to cavitation and a mistaken diagnosis of pulmonary abscess.

Pulmonary changes in rheumatoid arthritis are rare. Nodular or diffuse infiltrates with pleural effusions have been described.

It is estimated that 5–10 per cent of patients with scleroderma have pulmonary manifestations. Roentgenographically fibrosis, more marked at the bases, with honeycombing and pleural effusions is present. —*Barry E. Gerald, M.D.*

PUGSLEY, H. E., BROWN, A. S., and CHEUNG, O. T. Chronic cavitary histoplasmosis of the lung. *Canad. M. A. J.*, Mar. 30, 1963, *88*, 646–649. (From: Toronto Hospital for Tuberculosis, Weston, Ontario, Canada.)

Infection with *Histoplasma capsulatum* is rare in Canada, in contrast with its endemic status in many parts of the United States. The authors report 2 cases of chronic, cavitating pulmonary lesions originally diagnosed as tuberculosis but subsequently proven to be due to *H. capsulatum.*

The clinical course and roentgenographic findings are indistinguishable from those of tuberculosis. However, absence of a positive skin test and negative cultures for tuberculosis in the presence of a positive histoplasmin skin test is strongly suggestive of histoplasmosis. With cavitating lesions, the fungus can frequently be cultured. Treatment is with amphotericin B for at least 8 weeks with a total dose of 3 gm. If possible, resection of the involved area is done.

It is unlikely that the possibility of histoplasmosis would be overlooked in the mid-western or southern portions of the United States. The disease is being recognized, however, in other areas as well, as this article illustrates and can no longer be considered a regional problem.—*Barry E. Gerald, M.D.*

BORRIE, JOHN. Fifty thoracic hydatid cysts. *Brit. J. Surg.*, Nov., 1962, *50*, 268–287. (From: Department of Surgery, University of Otago, and Otago Hospital Board's Base Regional Thoracic Surgical Unit, Dunedin, New Zealand.)

The author reports 50 thoracic hydatid cysts removed from 40 patients. Of these, 45 were in the lungs, 3 in the anterior mediastinum, and 1 each in the pleural cavity and in the diaphragm. Sixty-six per cent (33) of those in the lungs were in the lower lobes.

The features of the disease included multiple involvement in 7 patients with no uniformity in distribution throughout the lungs. The cysts varied in size from 1 cm. to 10 cm., only 5 being less than 5 cm. in diameter. Cyst growth and size did not vary between children and adults. Thirty per cent (15) were shown to be ruptured at the time of removal, being due either to "quiet" rupture into a bronchus, sudden massive rupture, or a collapsed pericyst cavity following a previous rupture with chronic lung abscess. Daughter cysts occurred in 14 per cent (7). No calcifications were noted in this series. Pleural effusion was seen secondary to cyst rupture into the pleural cavity or simply due to infected cyst in the subjacent lung.

Clinically, 50 per cent had symptoms and signs of chest infection, 30 per cent had slight hemoptysis, while 18 per cent were detected after chance chest roentgenography. In 33 per cent, physical signs of a space occupying lesion were reported and 3 per cent had allergic phenomena.

Roentgenographically, 64 per cent showed a rounded or ovoid opacity in the chest or diaphragm. Other less frequent appearances were a visible membrane in a partially ruptured cyst in 4, a pericyst cavity following cyst evacuation in 3, an irregular opacity suggestive of neoplasm in 3, an inspissated lesion suggesting tuberculosis in 3, a fluid level in the lung in 3, a crescentic air shadow above a partly ruptured cyst in 1, and pleural effusion in 1.

Treatment was surgical in all but 3 cases, and ranged from cyst evacuation and suture in 33, lobar, segmental or wedge resection in 13, to total cyst excision in 1. Two patients died postoperatively, 1 from aspiration of vomitus and 1 from massive pulmonary embolus. Morbidity was essentially nil in the remainder.

Specific sensitivity tests are critically evaluated and difficulties in roentgen differential diagnosis are briefly discussed.—*Sam. B. Baker, M.D.*

Davis, Stanley, Gardner, Frances, and Qvist, George. The shape of a pleural effusion. *Brit. M. J.*, Feb. 16, 1963, *1*, 436–437. (From: Royal Free Hospital, London, England.)

The authors contend that neither the Ellis line of dullness nor the roentgenologic oblique line of density corresponds to the true upper limit of a free pleural effusion. They suggest that the true upper limit is horizontal and present 2 simple experiments to support their contention.

1. A coarse representation of the shape of a pleural effusion was made from a plaster cast. This was tapered in thickness from below upwards, but of uniform thickness in horizontal planes. In roentgenograms of this model with different penetrations, the line of density rises laterally until it reaches the true height of the plastic cast.

2. A plastic bucket was partially filled with water and an air-filled balloon was immersed in it. A roentgenogram was taken of this combination. Though the fluid was at the same level around the balloon, it was not possible to see the upper limits of the fluid in the central portion of the bucket. The fluid shadow is shown at a lower level extending upwards to the periphery until it coincides with the true fluid level.

In both cases, the rising line of density in the roentgenogram is, of course, due to the variation in depth of plaster and layer of fluid through which the roentgen rays passed toward the periphery. Fleischner (1926) suggested that the rising line of roentgenographic density can be explained by the axillary rays hitting the body more tangentially and having to pass through a greater thickness of fluid than the medial rays.

The authors conclude that the roentgen signs of fluid are misleading, and that the clinical signs are more accurate in estimating the extent of a pleural effusion.—*J. T. Ling, M.D.*

Williams, Bruce, Ling, Ji-Toong, Leight, Leonard, and McGaff, Charles J. Patent ductus arteriosus and osteoarthropathy. *A.M.A. Arch. Int. Med.*, Mar., 1963, *111*, 346–350. (From: Departments of Medicine and Radiology, University of Louisville School of Medicine, Louisville General Hospital, Louisville, Ky.)

A report of hypertrophic osteoarthropathy is presented, developing in a patient with a patent ductus arteriosus and reversed shunt. This is a rare complication of cyanotic congenital heart disease, occurring more commonly as a complication of pulmonary disease.

The patient, a 24 year old white female, had persistent ankle, knee, and pretibial edema, largely of the nonpitting type, accompanied intermittently by ankle and knee pain for the past 4 years. The absence of other manifestations of heart failure and the convincing roentgenographic findings all pointed to a diagnosis of hypertrophic osteoarthropathy.

The authors postulate that hypertrophic osteoarthropathy may result from chronic perfusion with hypoxic blood, since experimental osteoarthropathy has been produced in dogs after establishing arterial hypoxia.—*Francis P. Shea, M.D.*

Sanger, Paul W., Taylor, Frederick H., and Robicsek, Francis. Deformities of the anterior wall of the chest. *Surg., Gynec. & Obst.*, May, 1963, *116*, 515–522. (From: Department of Thoracic and Cardiovascular Surgery, Charlotte Memorial Hospital, Charlotte, N. C.)

Congenital deformities of the anterior wall of the chest are common. Rudimentary ribs, fusion and forking of costal cartilages, and aplasia of one or both pectoralis muscles usually have no clinical importance.

The arrested development of the sternum is an infrequent anomaly which may become a surgical problem. The failure of two cartilaginous bars to fuse results either in incomplete or complete separation. In most instances, the sternum can be united by simple approximation. The most common anomalies of the anterior portion of the chest belong to the chondrosternal depression (pectus excavatum) or chondrosternal prominence (pectus carinatum) group.

The authors believe that the displacement of the sternum is secondary and due to an overgrowth of the costal cartilages. If the sternum is pushed inward, pectus excavatum is the result; if it is pushed outward, pectus carinatum develops.

It is finally recognized that pectus excavatum and pectus carinatum are not harmless anatomic variants but are physiologically and psychologically crippling deformities. These anomalies should be treated surgically. Great controversy exists, however, as to which surgical methods offer the best results.

More than 30 different procedures have been described for the treatment of these anomalies. This shows that none of the advocated methods have proved entirely satisfactory.

The authors' technique for this correction is presented.

In *chondrosternal depression or pectus excavatum*, the method employed is a modification of the procedure described by Ravitch.

Chondrosternal prominence or pectus carinatum. The characteristic feature is protrusion of the sternum and costal cartilages as well as an increase of the retrosternal space. There are 3 main anatomic variants: 1. The first type is the symmetric protrusion of the sternum and costal cartilages; 2. the second variety is the lateral protrusion; 3. the third variety, chondromanubrial prominence in which only the manubrium and the first two costal cartilages are protruding, is an anomaly seldom encountered.

Chondromanubrial prominence with chondrogladiolar depression. The operation for the chondromanubrial deformity requires not only the repair of the prominence of the manubrium and the two upper cartilages but also alleviation of the depression of the body of the sternum.

Two hundred and twenty patients with deformities of the anterior portion of the chest were operated upon without any deaths.

Efforts to determine the disability of this disease by pulmonary function or hemodynamic studies have not been successful. Most patients are only vaguely conscious of their limitations. Only after operation are they aware of an improved status.

Optimal time for operation is considered to be between the ages of 2 and 6 years. Youth is not a deterrent.

Minor complications consisted of a few superficial wound infections, which responded well to drainage and antibiotic treatment.—*Stephen N. Tager, M.D.*

Meagher, Ronald P., Lupien, Jules, and Albert, Solomon N. Postoperative rupture of the esophagus. *Surg., Gynec. & Obst.*, Dec., 1962, *115*, 677–681. (From: The Department of Anesthesiology, Washington Hospital Center, Washington, D. C.)

The authors report 2 cases of spontaneous rupture of the esophagus associated with postoperative vomiting; they review the literature, and discuss the possible cause of this complication.

Two hundred and eighty-three cases of esophageal rupture have been collected from the literature, of which 25 cases were considered to have spontaneous rupture of the esophagus following postoperative vomiting.

The 2 patients reported are unusual in that the rupture was in the middle third of the esophagus rather than the distal portion. The first patient was a 58 year old female in whom the rupture occurred 18 hours following a pyelolithotomy. The second patient was a 53 year old white male in whom the rupture occurred 24 hours following a craniotomy for metastatic bronchogenic carcinoma to the brain.

The greatest incidence of spontaneous rupture of the esophagus is in 30–60 year old males; however, the over-all incidence ranges from 6 hours to 89 years. Most patients with this complication give a history of alcoholism or gastrointestinal tract disease associated with poor nutrition.

Two groups of underlying conditions are considered: (1) esophagomalacia associated with abnormal nervous stimulation, protein-metabolic disturbance or peptic injury; and (2) anatomic defects associated with weakness at the point of entry of neurovascular structures or muscular layers in the supracardiac portion of the lower third of the esophagus.

The usual precipitating factor is increased intraluminal pressure associated with vomiting and some abnormal stress. The increased pressure may be due to vomiting of large quantity of gastric contents and poor coordination with esophageal sphincters. Such a sphincter is found 1–2 cm. above the diaphragm, and it coincides with the most common site of rupture.

The usual pathologic finding is a 1–8 cm. longitudinal tear in the posterolateral aspect of the supracardiac esophagus. The tear may be into the mediastinum leading to mediastinal emphysema and mediastinitis or into the pleural cavity leading to pneumothorax and empyema.

The clinical findings include a rapid onset following vomiting with possible hematemesis, epigastric or substernal pain and a "tearing sensation" in the chest. There is early circulatory collapse, cyanosis, dyspnea, and cervical emphysema.

The treatment is surgical and should be carried out as early as possible. Roentgenologic examination facilitates early diagnosis and therapy and may reveal the location of the rupture. The survival rate is significantly higher when definitive treatment is accomplished within 24 hours.—*Gerald M. Wohlfeld, M.D.*

ABDOMEN

Texter, E. C., Jr., Van Derstappen, G., Chejfe, G., Chvojka, V. E., Vidinli, M., Barborka, C. J., and Bundesen, W. E. Criteria for the diagnosis of hiatal hernia. *A.M.A. Arch. Int. Med.*, Dec., 1962, *110*, 827–836. (From: Departments of Medicine and Radiology, Northwestern University Medical School, and the Medical and Radiology Services, Veterans Administration Research Hospital and Passavant Memorial Hospital, Chicago, Ill.)

The authors' report is based upon a study of several hundred patients with hiatal hernia. Fifty-seven patients underwent intensive study. The clinical features, routine and special roentgen studies, fluorocinematography, esophageal motility and perfusion studies, and endoscopy and endoscopic byopsy are assessed.

The ages of the 57 cases ranged from 35 to 81 years. The clinical manifestations are summarized. Seven patients were asymptomatic and 22 had accompanying disorders that could result in similar symptoms. A significant point was that there was no relationship between the severity of symptoms and the size of the hernia.

A hiatal hernia is defined as any condition in which the gastroesophageal junction is located above the diaphragm. The authors note that the landmarks for identifying the gastroesophageal junction have been revised within the last few years as a result of cinefluorographic studies. They specify that if the distal margin of the junction assumes a notched or ring configuration, a hernia exists.

Demonstration of a hernia or reflux can be accomplished in any variety of positions, but the authors favor the prone oblique swallowing technique. Employing this method, they were able to exceed the 50 per cent incidence reported by other authors.

Of 49 patients, esophageal motility studies demonstrated displacement of the physiologic gastroesophageal sphincter into the thorax in 26 patients; sphincter dysfunction in 27 patients; abnormalities of the deglutition pressure gradient in 46 patients; and spontaneous nonperistaltic motor activity in 27 patients.

In 26 patients who had heartburn, reproduced by perfusion of hydrochloric acid (the most effective agent), isotonic saline, or warm or cold water, there was simultaneous nonperistatic motor activity in 89 per cent. Apparently intraluminal esophageal pH, usually secondary to reflux, distention, and motor dysfunction, are significant in the production of heartburn.

Endoscopy demonstrated a hiatal hernia in 12 of 27 patients. The major value of this modality was in determining the extent and severity of the accompanying esophagitis.

The authors conclude that, for a given group of patients with a 10–30 per cent incidence of hiatal hernia determined by routine roentgen studies, an increased incidence will be found if special maneuvers, fluoroscopic spot filming, and newer criteria in interpretation are employed.—*Andre A. Galiber, M.D.*

Groves, Laurence K., and Effler, Donald B. Cancer of the gastric cardia associated with esophageal hiatus hernia. *Surg., Gynec. & Obst.*, April, 1963, *116*, 463–468. (From: Department of Thoracic Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio.)

Esophageal hiatus hernia is extremely common and dysphagia is frequently associated with it. On the other hand, dysphagia is the universal symptom of carcinoma of the esophagus or cardia of the stomach. The authors believe that the incidence of carcinoma is higher in cases with hiatus hernia, but they do not believe that this should be used as an argument to correct hernias for prophylactic reasons. Long standing peptic erosions may be a factor in producing malignant changes in the esophagus or cardia.

During a 12 year period, 12 patients with esophageal hiatus hernia and adenocarcinoma of the cardia were operated upon. These were among more than 500 patients surgically treated for hiatus hernia. Of these 12 patients, 4 had long histories of peptic distress typical of hiatus hernia. Symptoms were present up to 15 years. The other 8 had symptoms of less than 1 year's duration, and dysphagia was the common presenting complaint. These patients had few symptoms of the peptic type.

As surgeons, the authors believe that diagnosis of short esophagus may be erroneous. They point out that the entire subject of acquired and congenital short esophagus is controversial. Their series of 12 patients had adenocarcinomas only, although others have reported squamous cell carcinoma associated with hiatus hernia. The clinician should be aware of the frequency of the association of carcinoma and hiatus hernia so as to avoid errors of diagnosis and the subsequent penalties of therapeutic mismanagement.—*Richard E. Kinzer, M.D.*

Mathieson, Alister J. M. The Billroth-I recurrent ulcer. *Brit. J. Surg.*, Nov., 1962, *50*, 251–258. (From: Bridge of Earn Hospital, Perthshire, Scotland.)

The author reports on a series of 763 partial gastrectomies for duodenal ulcer performed during the years 1945–1958 at the Bridge of Earn Hospital, Perthshire. Of these, 375 were of the Pólya-type and 388 of the Billroth-I type. A rather standard type gastrectomy was done, involving removal of three-quarters of the stomach and with a stoma of not more than 2.5 cm.

Of this series, 43 patients or 5.6 per cent were known to have developed a recurrence: 39 patients, or 10.1 per cent were in the Billroth-I type and 4 patients, or 1.1 per cent in the Pólya-type anastomosis. The strict criteria for recurrence were (1) undisputed ulcer demonstrated roentgenologically; (2) ulcer found at re-operation. In this series, all recurrences were duodenal.

The author postulates a probable cause of recurrence after the Billroth-I operation as being due to ulceration of the duodenum, at least microscopically, present before operation.—*Keith Martin, M.D.*

Riordan, Arthur F., Bergmann, Karl, and Leslie, Eugene V. Bowel preparation for radiologic examination: comparison of techniques. *J. Canad. A. Radiologists*, Mar., 1963, *14*, 26–28. (From: Radiology Department, E. J. Meyer Memorial Hospital, Buffalo, N. Y.)

Since the barium enema examination requires the most meticulous cleansing preparation, the authors studied and compared the effectiveness of bisacodyl tablets and suppositories (Dulcolax by Geigy Laboratories) with castor oil and enemas. A total of 358 barium enema studies were included in this group. Bisacodyl is a colorless, tasteless and odorless compound with a therapeutic-toxic ratio of 1:200. It is a true contact laxative, acting upon the nerve endings in the colonic mucosa. The drug has little action on the small bowel. Undesirable side effects have not been noted.

The patients were divided into four preparation groups. Group I received 3 oral tablets of bisacodyl and a rectal suppository the evening prior to the examination, and another suppository the morning of the examination. Group II received one and one-half ounces of castor oil at 4:00 P.M. on the day prior to the examination, and a bisacodyl suppository at 11:00 P.M. and at 7:00 A.M. Group III and Group IV received routine preparation of one and one-half ounces of castor oil at 4:00 P.M. the day before and then, in the morning, cleansing tap water enemas until the return was clear. Group III was composed of in-patients while Group IV represented the out-patients who were included early in the study.

One observer, who was unaware of the type of preparation the patient received, evaluated the barium enema roentgenograms. Several other observers acted as dual evaluators with notable agreement prevailing. The success of the preparation was classified as excellent, good, fair and poor.

The average age of the patients was 61.0 years and their age distribution was markedly skewed toward the later decades of life. This adversely influenced the effectiveness of all of the preparations employed. Those patients who received bisacodyl in any form as a part of their preparation and whose barium enema examinations were repeated because of poor cleansing, were prepared for the repeat barium enema study with castor oil and cleansing enemas. In this group there was no appreciable change in the grade of bowel preparation, suggesting that the poor preparation was dependent more on patient than on the method of preparation.

An average of 40 minutes was consumed in the administration of the cleansing enemas on the wards and this time varied from 15 to 90 minutes. When one balances the cost of the suppositories against the expense and the inconvenience of administering the cleansing enemas, it can be seen that bisacodyl suppositories are considerably more economical. A low residue diet for one to several days prior to examination was of great value especially for the recalcitrant patient.

One third of the patients in Group I (tablets and suppositories) had unsatisfactory preparation. The results in Group II (castor oil and suppositories) and Group III (castor oil and enemas) showed no statistical difference in the results of bowel preparation. The first three grades of all Groups were satisfactory for diagnostic purposes in most instances.—*J. N. Ané, M.D.*

FLEMMA, ROBERT J., SCHAUBLE, JAMES F., GARDNER, CLARENCE E., JR., ANLYAN, WILLIAM G., and CAPP, M. PAUL. Percutaneous transhepatic cholangiography in the differential diagnosis of jaundice. *Surg., Gynec. & Obst.*, May, 1963, *116*, 559-568. (From: Departments of Surgery and Radiology, Duke University Medical Center, Durham, N. C.)

The authors employed percutaneous transhepatic cholangiography in 47 cases and believe that this procedure reveals the pathologic anatomy of the biliary tree more precisely than any other test known at present. It is possible to differentiate obstruction due to stone from that secondary to carcinoma; to locate the point of obstruction from benign stricture; and when carcinoma involves the pancreas or the bile ducts, besides locating the level of the obstruction preoperatively, this method of study indicates the type of feasible by-pass procedure. The hazard of biliary leakage from the puncture site has been pointed out. The procedure should be performed when the patient is prepared for possible surgery and the surgical team should be available to maintain a close watch for signs of peritoneal irritation.

After careful preliminary medication, tests and local anesthesia a No. 18 aortogram needle was introduced in the midclavicular line, immediately below the costal margin. The needle was quickly inserted to a depth of 12 cm., at a 45 degree angle to the horizontal and aimed 20 degrees to the left of the midclavicular line, during suspended respiration. The patient was allowed, then, to breathe. With syringe attached the needle was withdrawn very slowly while it was rotated constantly with suction applied. If blood was aspirated the syringe and the needle were flushed with saline and the needle was withdrawn very cautiously since bile ducts are often entered just after withdrawal from a blood vessel. If a bile duct was not entered in four punctures the authors assumed that there was no extrahepatic obstruction. Although Glenn demonstrated a normal biliary tree in such a case, on one occasion the authors have never been able to do so. Once a bile duct was entered bile was drawn off for cytologic and bacteriologic study and hypaque, 50 per cent was then introduced. Between 20 to 60 cc. of hypaque was employed and spot roentgenograms during injection were made. Multiple views of the abdomen were used. After roentgenography, the opaque medium and as much bile as possible were withdrawn if complete obstruction was demonstrated. Antibiotics were continued and a close watch was maintained over the patient. In 3 cases of the authors' series emergency operative intervention was required.

Seventeen patients of the group, who were examined by percutaneous transhepatic cholangiography, had carcinoma of the head of the pancreas. The characteristics were as follows: (1) a greatly dilated common duct, (2) a rounded configuration at the distal end of the common duct with the meniscus of the opaque medium projecting inferiorly and (3) complete obstruction to flow of opaque medium as shown by absence of hypaque in the gastrointestinal tract.

Choledocholithiasis with obstruction at the ampulla of Vater presented the following findings: (1)

the meniscus of the opaque medium is convex upward and outlines the superior part of the stone, (2) small amounts of the opaque medium pass around the stone into the duodenum and (3) dilatation of the duct is not as great as that noted with carcinoma. In benign strictures this procedure is the method of choice.—*J. N. Ané, M.D.*

ARCOMANO, JOSEPH P., HEROY, WILLIAM W., and BARNETT, JAMES C. Fixed filling defects of the gallbladder. *Am. J. Digest. Dis.*, Mar., 1963, *8*, 222–234. (Address: Department of Radiology, The North Shore Medical Group, 325 Park Avenue, Huntington, L.I., N. Y.)

Twenty-seven cases of fixed filling defects of the gallbladder are described, 17 of which came to surgery. Recent classifications of these lesions by Jones and by Jutras tend to point up the confusion in terminology.

The authors prefer Jutras' classification of the hyperplastic cholecystoses because it emphasizes the pathogenesis and response to stimuli. It is agreed that carcinoma is still usually diagnosed in retrospect. Multinodular lesions restricted to the fundus will almost always be the lesions of adenomyosis (hyperplasia glandularis proliferans) when there is the halo of intramural diverticula about them. A solitary nodule without umbilication or accompanying diverticula is usually an adenomatous polyp. Multipolypoid lesions of various sizes in any region of the gallbladder generally constitute cholesterolosis.

The reader is referred to the original article for a detailed description of each entity and a review of the literature.—*Arch H. Hall, M.D.*

PITMAN, R. G., and DAVIES, ALAN. The clinical and radiological features of spontaneous internal biliary fistulae. *Brit. J. Surg.*, Jan., 1963, *50*, 414–425. (Address: Cardiff Royal Infirmary, Cardiff, Wales.)

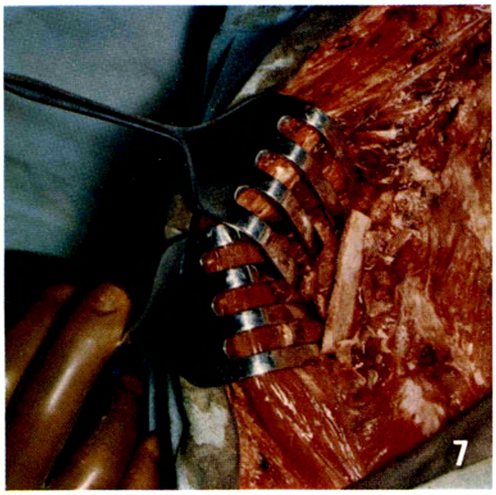
A spontaneous internal biliary fistula connects the extrahepatic biliary tract with another abdominal viscus, usually the stomach, duodenum, or colon. It is called spontaneous when it is unrelated to surgery or trauma. The authors quote a series of 819 cases reviewed by Waggoner and Le Mone (1949) in which it was found that 51 per cent were cholecystoduodenal, 21 per cent cholecystocolic, and 19 per cent choledochoduodenal fistulae. Rarer types are cholecystogastric, choledochogastric, and cholecystocholedochal fistulae. Gallstones are associated with approximately 90 per cent of the fistulae which primarily involve the gallbladder. The penetrating duodenal ulcer accounts for 6 per cent and involves the common bile duct. The penetrating ulcer is the cause of 80 per cent of the choledochoduodenal type of fistula.

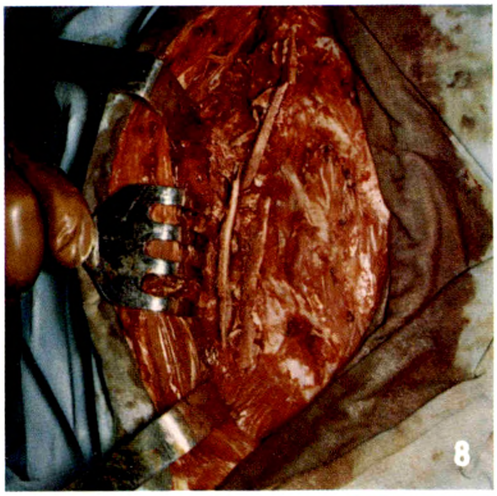
The roentgen features may be divided into those revealed by a plain roentgenogram of the abdomen and those demonstrated by the use of contrast media. Biliary gas may be visible in the right upper quadrant in the pattern of the bile ducts. This is likely to occur when there is a choledochoduodenal fistula or a choledochoenterostomy, or an incompetent sphincter of Oddi. When there is a cholecystenteric fistula or a cholecystoenterostomy, the common bile duct rarely contains gas and only small amounts are present in the intrahepatic radicles. Biliary gas is visible on roentgenograms made in both the erect and supine positions. In the erect position, however, it may be demonstrated when none is visible on the supine roentgenogram. When the plain roentgenogram is doubtful, gas may be introduced by having the patient swallow an effervescent drink, and placing him in the supine position with his right side raised off the table. This allows the gas to fill the pyloric antrum and the duodenum. This method has the following advantages: (1) gas in the bile ducts is harmless; (2) it may increase the volume of gas in the bile ducts, thereby confirming that gas can enter the ducts; and (3) it may outline the ducts well enough to confirm or exclude the presence of an opaque gallstone in the ducts.

A barium meal examination may reveal similar findings as gas, except that the ducts or gallbladder may contain barium. However, if a fistula is suspected it is safer to use an absorbable contrast material than a barium meal. A barium enema study may also show barium in the gallbladder or ducts if there is a fistula between the colon and the biliary tract. Cholangiograms made at surgery may be helpful in outlining a fistula.

The authors give 9 case reports with a discussion of the clinical features, complications and management. There are a number of excellent reproductions of roentgenograms included, illustrating the roentgen features discussed.—*Douglas S. Kellogg, M.D.*

2ND STAGE POSTEROLATERAL FUSION *(continued)*





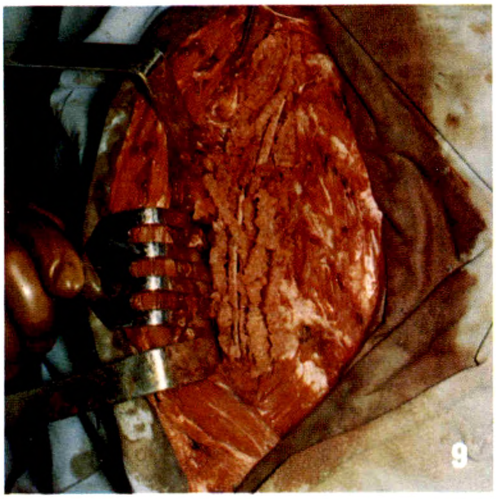


Figure 7. Autogenous corticocancellous graft inlaid into slots in fusion bed at T-12 and L-1.

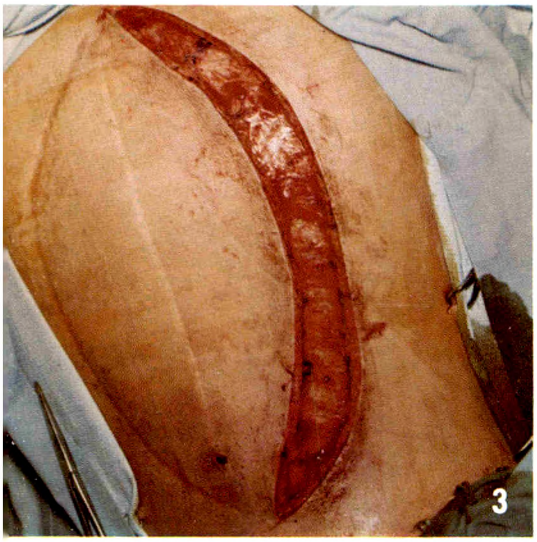
Figure 8. Same as Figure 7 continued proximally to T-9.

Figure 9. Fusion mass reinforced with sliver grafts; wound now ready for closure.

LOOK TO KODAK for color film: Kodachrome II, Kodachrome II Professional, Kodachrome-X Films for miniature cameras; high-speed Kodak Ektachrome ER Film for 16mm motion-picture cameras; Kodak Ektachrome-X Film and Kodacolor Film for roll-film and miniature cameras; Kodak High Speed Ektachrome Film for miniature cameras. Kodak Ektacolor and Kodak Ektachrome Films for sheet-film cameras; also Kodak color print materials in wide variety.

Kodak
TRADEMARK

Patient was young married woman who required operation because of increasing round back deformity due to a congenital blood vessel abnormality of the spinal cord. This followed acute paralysis requiring extensive decompression of the spinal cord and consequent loss of bony support in the thoracolumbar area, thus forcing spinal fusion from the sides.



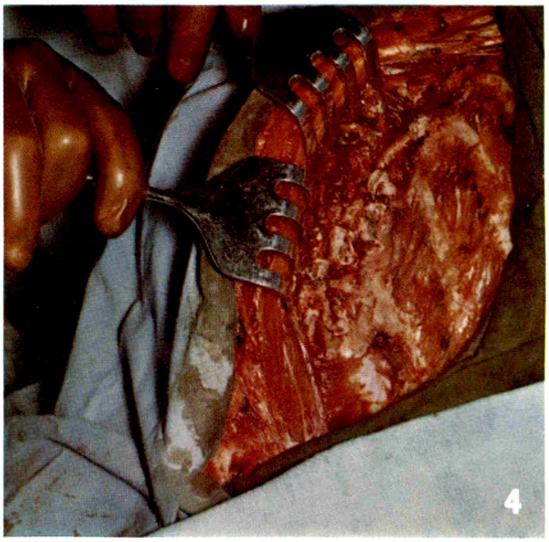
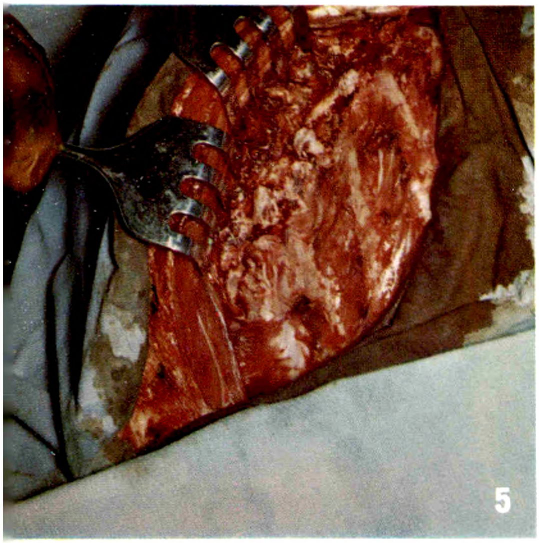


Figure 3. Right curvilinear incision T-8 to L-2.
Figure 4. Transverse and articular processes and ribs T-9 through L-1 before preparing fusion bed. Incised lumbodorsal fascia, trapezius, serratus posterior inferior and longissimus (muscles) retracted medially.



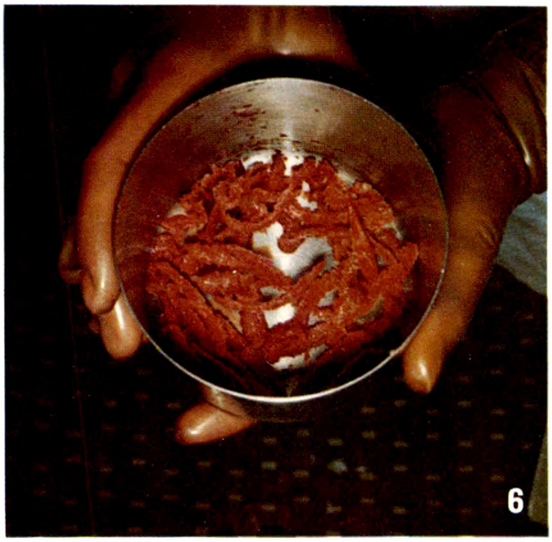


Figure 5. Transverse and articular processes and ribs T-9 through L-1 after preparing fusion bed.

Figure 6. Slivers of cancellous bone (autografts) obtained from posterior superior iliac crest.

FOR FURTHER DETAILS—TURN PAGE.

FOR YOUR FILES . . . Cut along this line

2nd STAGE POSTEROLATERAL FUSION: Surgical correction of an extensive laminectomy defect.

2nd stage posterolateral fusion (T-9 to L-1 inclusive) for painful kyphotic deformity following extensive laminectomy for congenital varices of the thoracolumbar cord.

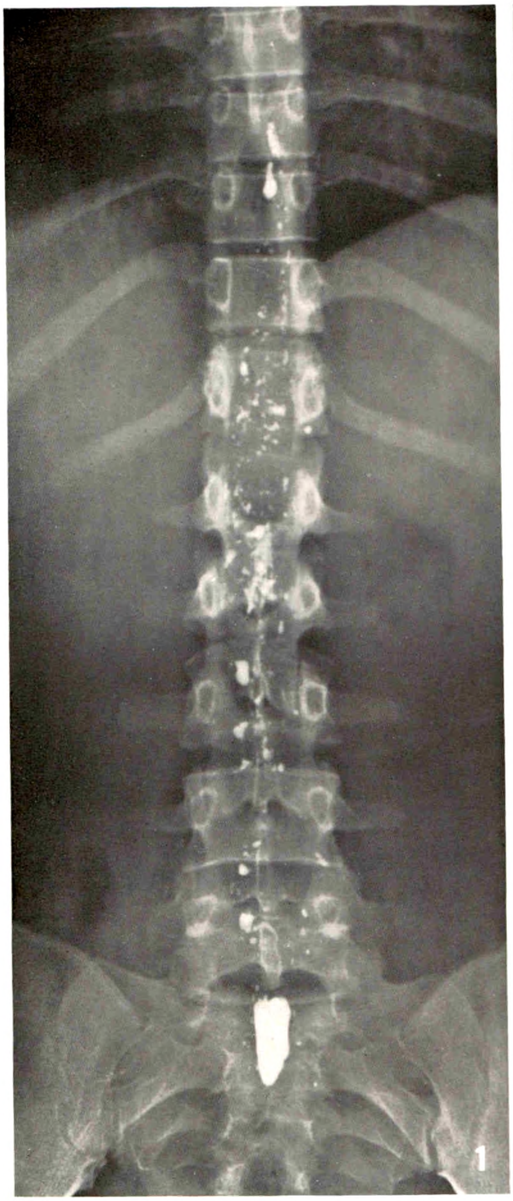


Figure 1. *Preoperative anteroposterior radiograph* shows extensive laminectomy defect, T-9 through T-12 inclusive, with absence of articular facets between T-12 and L-1.

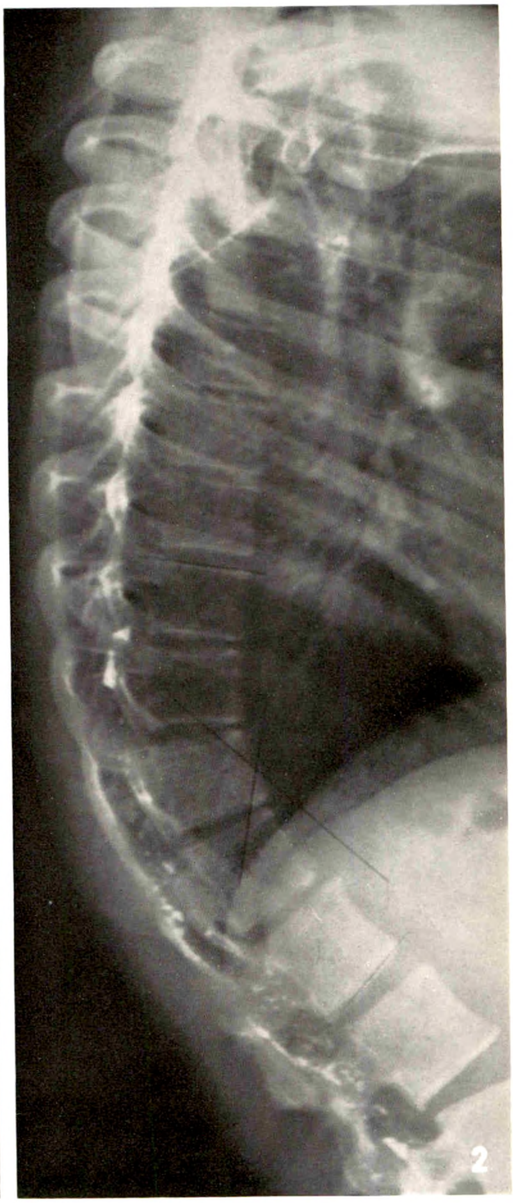


Figure 2. *Preoperative lateral radiograph.* Note kyphotic deformity secondary to bony instability. Laminectomy had been performed for bleeding due to congenital spinal cord varices.

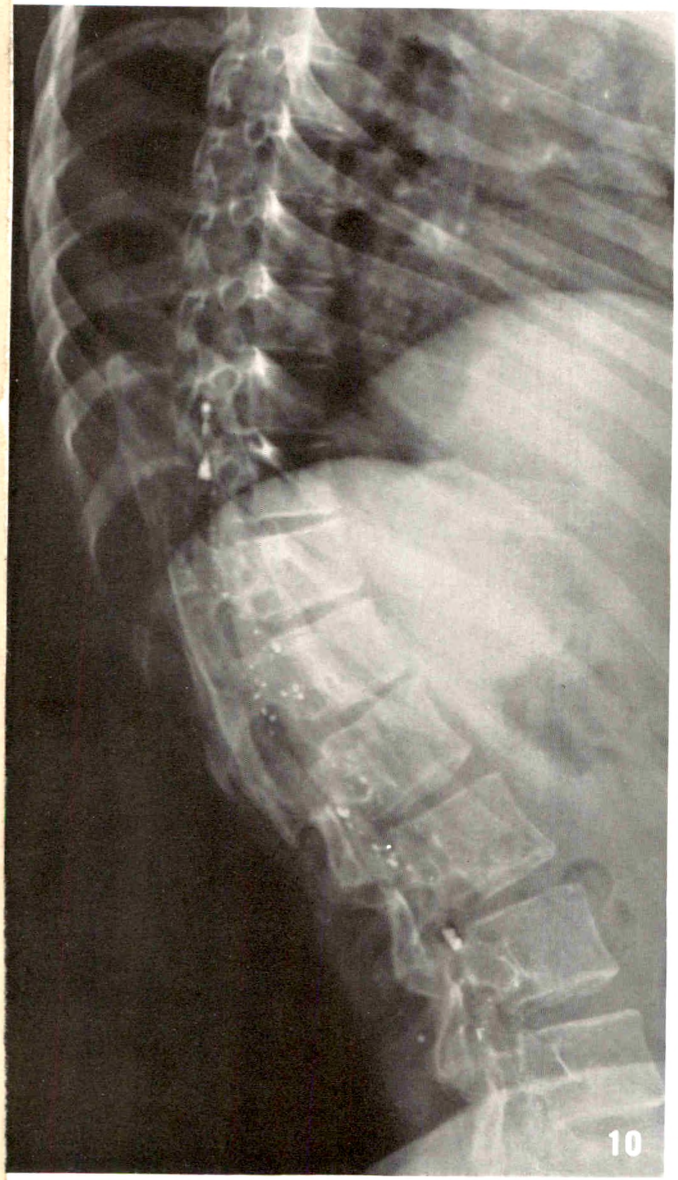


Figure 10. *Postoperative radiograph*, slightly oblique lateral view. Note strong bony stabilization of involved area by fusion bilaterally of costotransverse and articular processes.

Preoperative and postoperative radiographs on Kodak Royal Blue Medical X-ray Film; surgery photographed on Kodak Ektachrome Film.

Reprints available upon request. Write to address below stating quantity desired.

FOR RADIOGRAPHS of highest quality . . . Look to Kodak for medical x-ray film . . . Kodak Royal Blue, Kodak's fastest, and Kodak Blue Brand.

Order KODAK x-ray products from your Kodak x-ray dealer
Order KODAK photographic products from your Kodak photographic dealer

X-ray Sales Division, EASTMAN KODAK COMPANY, Rochester 4, N.Y.

2nd World Congress of Gastroenterology
Munich 1962

Praeses: N. HENNING, Erlangen—Curator: E. SCHMID, Erlangen

Vol. I: Topical Problems in Achalasia of the Oesophagus
Editores: F. J. INGELFINGER (Boston, Mass.); G. SIFFERT (Rio de Janeiro). XL + 143 p., 43 fig., 14 tab., 1963. US $8.40

Vol. II: Topical Problems in Diseases of the Alimentary Tract
Editores: E. SCHMID (Erlangen); J. TOMENIUS (Stockholm); G. WATKINSON (Leeds). XL + 880 p., 345 fig., 80 tab., 1963. US $40.80

Vol. III: Topical Problems in Diseases of the Liver
Editores: L. DEMLING (Stuttgart); M. DEMOLE (Genf); H. POPPER (New York). XL + 672 p., 225 fig., 75 tab., 1963. US $33.60

Vol. IV: Topical Problems in Pancreatitis
Editores: H. BARTELHEIMER (Hamburg); H. LAGERLÖF (Stockholm). XL + 172 p., 47 fig., 21 tab., 1963. US $9.60

Vol. V: Gastro-enterological Aspects of other Diseases
Editores: H. BERNING (Hamburg); K. SPANG (Stuttgart). XL + 144 p., 24 fig., 9 tab., 1963. US $8.40

Complete Proceedings, Part I-IV: CC + 2011 p., 684 fig., 199 tab., 1963. US $80.65

Additional publication:

Malabsorption Syndromes

Symposium held at the Second World Congress of Gastroenterology, Munich, May 19th, 1962

Editor: H. SCHÖN (Erlangen)
IV + 116 p., 19 fig., 14 tab., 1963. US $5.75

Please ask for prospectus

S. KARGER AG, Arnold-Böcklin-Strasse 25, BASEL (Switzerland)

Please send me ....

Name ....

Address ....

Please place your order with:

ALBERT J. PHIEBIG, P.O. Box 352, White Plains, N.Y.

BRITISH JOURNAL OF RADIOLOGY

SUPPLEMENT No. 9

THE SPECTRA OF X RAYS SCATTERED IN LOW ATOMIC NUMBER MATERIALS

By W. R. Bruce, M.D., Ph.D., and H. E. Johns, Ph.D., F.R.S.C.

The complicated effects of multiple scattering have always presented a major difficulty to analysts of X-ray beams traversing matter. In this Supplement the authors describe how the Monte Carlo method of computation may be used to allow for multiple scattering when studying the penetration of X-ray beams. A full discussion of their combination of analytical and Monte Carlo methods is presented and much information on the spectra of X-ray beams in the photon energy range from 50 to 1250 ke V is provided in the form of graphs and tables, with the main emphasis on data for beams traversing water. This Supplement will interest all those concerned with the use of X rays in radiotherapy and in radiobiological studies.

Price: 12*s.* 6*d.* \$2.00 (One copy is allowed to each member at 7/6*d*—*U.S.A.* \$1.50)

SUPPLEMENT No. 10

DEPTH DOSE TABLES FOR USE IN RADIOTHERAPY

(containing 77 tables, three full-page and two half-page graphs)

The value of central axis depth dose and related data in radiotherapy was evident from the heavy demand made for *Supplement No. 5* (1953), “Central Axis Depth Dose Data”. When stocks of the latter were exhausted three years ago, it was decided to revise the original data in the light of more recent experimental work, and to extend the coverage to the higher energies now coming into general use. This task was undertaken by the Scientific Subcommittee of the Hospital Physicists’ Association.

The new edition contains nine main sections covering electromagnetic radiations ranging from Grenz rays (H.V.T. 0.01 mm of Al) up to 31 MV betatron X-rays, and including electron beams (2 to 30 MeV). Every effort has been made to ensure that tables are adequately explained as to origin, possible sources of error and limitations of applicability. Where significant differences from the earlier data occur, they are discussed by the individual reviewers of the sections concerned.

This Supplement provides the most comprehensive selection of central axis data in existence, and has been compiled by acknowledged experts in the field.

Price: 45*s.* \$7.50 (One copy is allowed to each member at 32/6*d*—*U.S.A.* \$6.50)

obtainable from

THE BRITISH INSTITUTE OF RADIOLOGY
32 WELBECK STREET, LONDON, W.1
and from leading booksellers all over the world

The Beaumont Lecture
Wayne County Medical Society
Detroit, Michigan

Changing Perspectives on the Genetic Effects of Radiation

One of the most widely discussed scientific problems of our times concerns probable deleterious effects of mankind's increasing exposure to ionizing radiation. *In this monograph Doctor Neel considers perhaps the most controversial aspect of this problem* . . . **the question of genetic damage.**

The author reviews first extensive studies which he himself directed on genetic effects of the atomic bombs in Hiroshima and Nagasaki. He focuses particular attention on the validity of the small change in sex ratio among children born to exposed parents—not only in Hiroshima and Nagasaki but in a number of studies carried out elsewhere in the world.

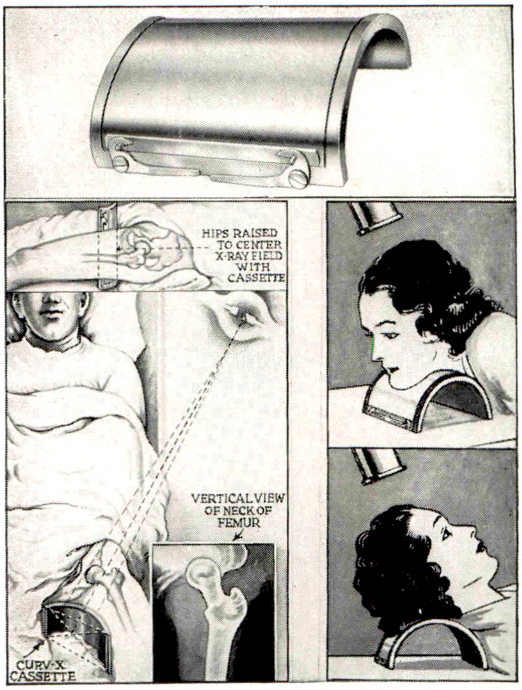
By
JAMES V. NEEL
Department of Human Genetics
University of Michigan Medical School
Ann Arbor, Michigan

The role of radiation in producing leukemia as well as visible damage to the chromosomes of somatic cells is reviewed and pertinence of these data to the genetic picture emphasized. In the final section Doctor Neel develops a perspective on the magnitude of the threat posed by man's growing exposure to radiation.

March 1963 *112 pages*
$5.00 *22 illustrations*

CHARLES C THOMAS • PUBLISHER
301-327 East Lawrence Avenue
Springfield • Illinois

THE CURV-X CASSETTE


HIPS RAISED TO CENTER X-RAY FIELD WITH CASSETTE
VERTICAL VIEW OF NECK OF FEMUR
CURV-X CASSETTE

CAMPBELL X-RAY-TRANSFORMER CO., INC.
Malden 48, Mass. Or Your Dealer

In reply to advertisers please mention that you saw their advertisement in THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE.

•

CHARLES C THOMAS · PUBLISHER
Springfield · Illinois

HANLEY ECONOMY 14x17 X-RAY CABINET
SPECIAL DESIGN SLIDING DOORS
QUALITY AT LOW PRICES
Vertical Filing
We Build Special Size X-Ray Cabinets
5 COMPARTMENT SIZE—DIVIDERS 14 x 17 ....$114.70
3 COMPARTMENT SIZE—DIVIDERS 14 x 17 .... 90.00
APPROVAL GUARANTEED—F.O.B. FACTORY—CATALOGUE
HANLEY MEDICAL EQUIPMENT CO.
5614 South Grand X-ray Division St. Louis 11, Mo.

Full-time staff position available in Radiology Service in 1238 bed Veterans Administration Hospital. Program fully integrated with New York University Bellevue Medical Center. Active Gastrointestinal, Pulmonary and Neuro Radiology services. Ample opportunity for research. Salary up to $18,405. Contact Chief, Radiology Service, Veterans Administration Hospital, First Avenue at East 24th Street, New York 10, New York.

Veterans Administration Full-time Staff

INDEX TO ADVERTISERS

Allis-Chalmers Mfg. Company ... li
Ansco (General Aniline & Film Corp.) ... xxviii, xxix
Associated Electrical Industries ... xl, xli
Atomic Energy of Canada Ltd. ... xxv
Automatic Seriograph Corp. ... Second cover

Barnes-Hind Barium Products ... xlii, xliii
Bell-Craig, Inc. ... liii
British Institute of Radiology ... lxii

Campbell X-Ray Corporation ... lxiii
Canadian Association of Radiologists ... lxv
Continental X-Ray Corporation ... xlvi

Dunlee Corporation ... xxxiii
du Pont, E. I. de Nemours & Co. (Inc.) ... ix, x xi, xii

Eastman Kodak Company ... lvii, lviii, lix, lx
E-Z-Em Company ... xlviii

Fougera, E. & Company, Inc. ... Third cover

Geigy Pharmaceuticals ... vi
General Electric Company ... xx, xxi, xxii, xxiii, xliv, xlv

Halsey X-Ray Corporation ... xxxiv
Hanley Medical Equipment Company ... lxiii
Hunt, Philip A. Company ... xlvii

Ilford, Inc. ... xxvi, xxvii

Karger, S. ... lxi
Keleket X-Ray Corporation ... xvi, xvii

Lea & Febiger ... lxvi
Liebel-Flarsheim (Division of The Ritter Co., Inc.) ... xxxv
Low X-Ray Corporation ... xix

Machlett Laboratories ... xiii
Mallinckrodt Chemical Works ... xxxvi, xxxvii
McElroy, Donald, Inc. ... lii
Mitchell X-Ray Products ... xviii

Nuclear-Chicago Corporation ... xiv, xv

Olympic Surgical Company ... l

Philips, N. V., Gl. ... xxiv
Picker X-Ray Corporation ... vii, xxxi, xxxii, Fourth cover
Profexray, Inc. ... i

Record Files, Inc. ... lxv

Siemens America, Inc. ... xlix
Squibb, E. R. & Sons ... v
Standard X-Ray Company ... lv

Thomas, Charles C, Publisher ... liv, lxiii

Urell, Inc. ... lii
U. S. Radium Corporation ... xxx

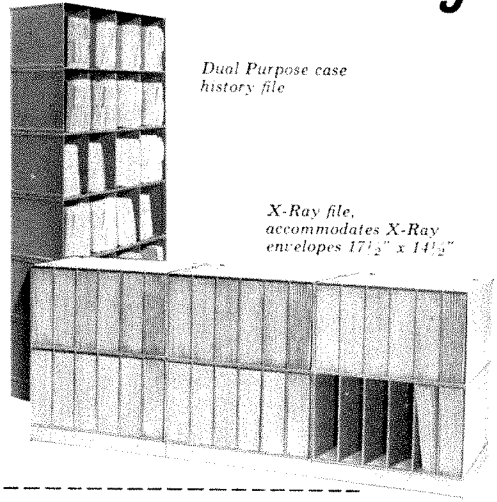
Varian Associates ... xxxviii, xxxix
Veterans Administration Hospital ... lxiii

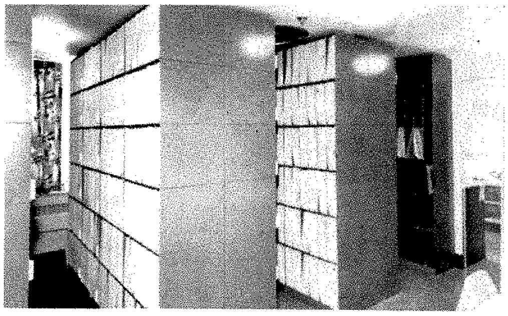
Westinghouse Electric Corporation ... lvi
Winthrop Laboratories ... viii

●

We try to present an accurate index. Occasionally this may not be possible because of a last-minute change or an omission.

RFI Files In Leading Medical Institutions


Dual Purpose case history file
X-Ray file, accommodates X-Ray envelopes 17½" x 14½"


X-Ray file installation at Robinson Memorial Portage County Hospital, Ravenna, Ohio

RFI storage files are conspicuous for their "repeated presence" in the country's leading medical institutions. Medical record librarians have grown to depend on the completeness of the RFI line. They know RFI has the file for their specific needs, or that RFI engineers will design it for them. Here are two of the more popular RFI units — the X-ray storage file and the case history file in letter or legal size. Both have interlocking features and structural strength to give many years of trouble-free service. All RFI files stack as high as you wish to give greater storage capacity in fewer square feet of floor space. Many other sizes and styles are available — write for our catalogue.

RECORD FILES, INC. Dept. RJI
P.O. Box 581
Wooster, Ohio

Please send me complete information on RFI files for medical institutions.

Name____________________

Address____________________

City____________ State____________

RECORD FILES INC. WOOSTER, OHIO RFi

Canadian Association of Radiologists
L'Association Canadienne des Radiologistes

Subscribe today to

THE JOURNAL OF THE CANADIAN ASSOCIATION OF RADIOLOGISTS

published quarterly: March, June, September and December. It is the **official organ** of **The Canadian Association of Radiologists.**

Price $3.50 per annum in Canadian or equivalent funds.

The Canadian Association of Radiologists,
1555 Summerhill Avenue,
Montreal 25, Quebec, Canada

Please enter my subscription to the JOURNAL OF THE CANADIAN ASSOCIATION OF RADIOLOGISTS, for which my cheque is enclosed.

Name ....
(Please print)

Address ....
(Please print)

City .... Province or State .... Country ....

The Electrocardiogram and Chest X-Ray in Diseases of the Heart

New!

By ARTHUR M. MASTER, M.D.
Consultant Cardiologist, The Mt. Sinai Hospital, New York City
RICHARD P. LASSER, M.D.
Assistant Attending Physician for Cardiology,
The Mt. Sinai Hospital, New York City
ISADORE ROSENFELD, M.D.
Instructor in Medicine, Cornell Medical College, New York City
and EPHRAIM DONOSO, M.D.
Assistant Attending Physician for Cardiology,
The Mt. Sinai Hospital, New York City

376 Illustrations!

ROENTGENOGRAPHIC, electrocardiographic, clinical and pathophysiologic findings in a wide variety of cardiac diseases are presented in this up to date, authoritative work. Emphasis is on pictorial representation. Almost 400 illustrations, x-rays and electrocardiograms provide a useful visual association with the clearly worded text. After a comprehensive account of the normal teleoroentgenogram and electrocardiogram, and of the more important ancillary techniques which facilitate their interpretation, there is a broad, general description of cardiac chamber enlargement and a consideration of the general principles of "Chamber stress." Characteristic roentgen and electrocardiographic findings are related to the underlying hemodynamic abnormalities. Specific disease entities are described in terms of their clinical, pathophysiological, roentgenologic and electrocardiographic characteristics.

565 Pages, 7″ × 10″. 376 Illus. on 139 Figs. 119 Case Histories. New. $21.00

LEA & FEBIGER **Washington Square, Philadelphia, Pa. 19106**

Please enter my order and send me:

Master, Lasser, Rosenfeld and Donoso—Electrocardiogram and Chest X-Ray $21.00

☐ Check enclosed. Bill me at ☐ 30, ☐ 60, ☐ 90 days. ☐ Charge on your monthly payment plan.
(We pay postage if remittance in full accompanies your order)

NAME (print) ....

ADDRESS ....

CITY .... STATE .... ZIP NO. ....

Am. Jl. R., RT & N.M. 10-63

FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

OFFICIAL ORGAN OF
THE AMERICAN ROENTGEN RAY SOCIETY
THE AMERICAN RADIUM SOCIETY

CALCUTTA UNIVERSITY
CENTRAL LIBRARY

TRAIAN LEUCUTIA, Editor
KENNETH L. KRABBENHOFT, Assistant to the Editor

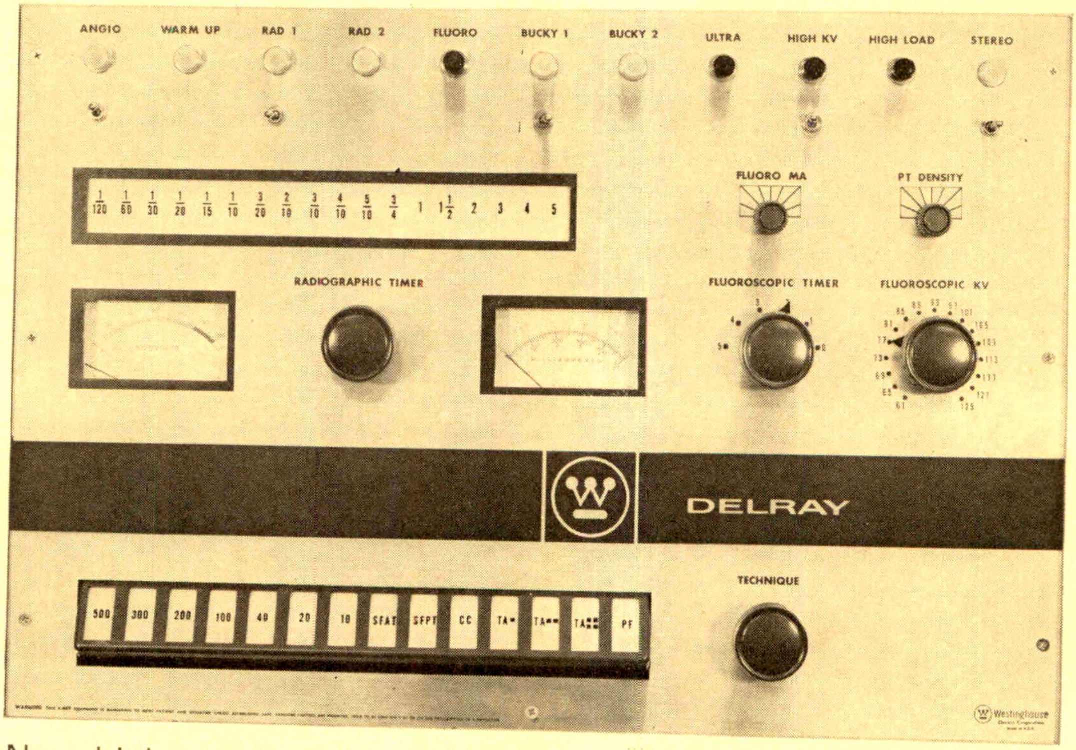
ASSOCIATE EDITORS
HARRY HAUSER RUSSELL H. MORGAN EDWARD B. D. NEUHAUSER
WENDELL G. SCOTT

CONSULTING EDITORIAL BOARD
PAUL C. AEBERSOLD
OSCAR V. BATSON
JOHN CAFFEY
ROSS GOLDEN
PAUL C. HODGES
HOWARD B. HUNT
JOHN H. LAWRENCE
REED M. NESBIT
EUGENE P. PENDERGRASS
U. V. PORTMANN
LAURISTON S. TAYLOR
OWEN H. WANGENSTEEN
SHIELDS WARREN

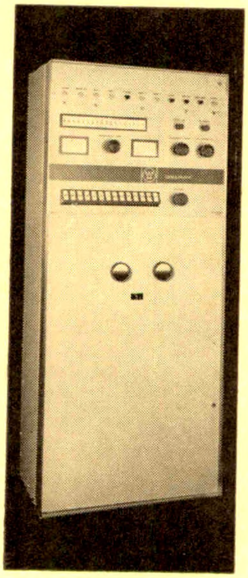
Issued Monthly for the American Roentgen Ray Society by
CHARLES C THOMAS · PUBLISHER · SPRINGFIELD · ILLINOIS

VOLUME 90 NOVEMBER, 1963 NUMBER 5

Within this control, reliability by Westinghouse:



Now, high-speed anode rotation for high kv technique with the all NEW DELRAY CONTROL. Anode rotation at standard speeds or as high as 10,000 rpm. 500 ma-150 kv, 300 ma-150 kv and 125 kv.



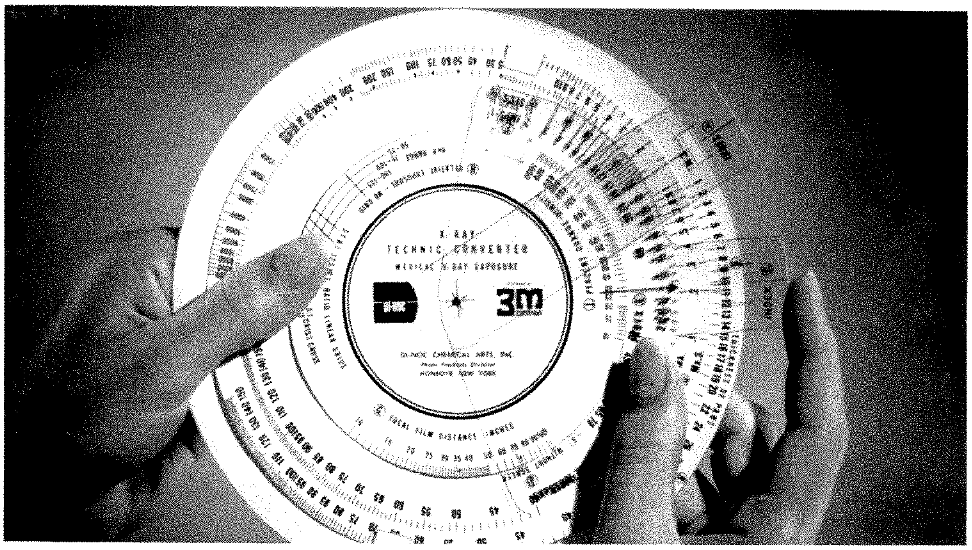
■ Compact, space-saving design. Clean, modern styling. ■ Eye-level indicators and efficient control grouping for quick, easy, accurate operation. ■ Engineered for total flexibility with circuitry arranged to accommodate all techniques—including high kv. ■ Plug-in relays are lifetime-sealed. ■ Simplified design for fast, easy installation and service. ■ For full technical data, write Westinghouse Electric Corporation, X-Ray Division, 2519 Wilkens Avenue, Baltimore 3, Maryland.

You can be sure . . . if it's Westinghouse.

We never forget how much you rely on Westinghouse

J-08413-A

DI-NOC ANNOUNCES MEDICAL X-RAY TECHNIC CONVERTER



Now...make your x-ray technic conversions easier, faster!

Now those complex technic conversions for every x-ray situation can be quickly and accurately made with Di-Noc's new converter. Minimizes re-takes, reduces exposure, saves film and time. Easy to use.

MANY IMPORTANT BENEFITS

- For variations in size of patients when using low or high voltages (with or without intensifying screens), the correct Kv.P. or Ma.S. is determined.
- When changing from one type screen to another, or from screen to no-screen technic, adjustment in Kv.P. or Ma.S. is shown.
- For changing either Kv.P. or Ma.S. without altering density, correct compensation is indicated.
- For changes in target-film distance, the adjustment required in Kv.P. or Ma.S. is indicated.
- For changes in type of grid used at different voltages—or change to a non-grid technic—the necessary variation in Kv.P. or Ma.S. is shown.
- To adjust density at low or high voltages, with or without screens, necessary change in Kv.P. or Ma.S. is indicated.
- To obtain specific Ma.S., the combinations of Ma. and time required are shown.

COMPLETE INSTRUCTIONS included with each converter. All scales based upon most accurate and scientific data available. Exhaustive tests prove accuracy and tremendous value of this converter. Order your converter now. Satisfaction guaranteed.

ORDER FROM YOUR DEALER OR DIRECT

DI-NOC CHEMICAL ARTS, INC.
PHOTO PRODUCTS DIVISION
EAST LAKE ROAD, HONEOYE, N. Y.

Send me__________Medical X-Ray Exposure Technic Converters at $9.75 each, postpaid. My check enclosed.

Name____________________

Address____________________

City__________ Zone____ State________

Di-Noc Chemical Arts, Inc. 3M
A SUBSIDIARY OF 3M COMPANY

SYMBOL OF THE BEST IN ROENTGENOLOGY

5 New Books Published in 1963 . . .

☐ **THE PRACTICE OF COUNTRY RADIOLOGY** by Donald de Forest Bauer, Klamath Valley Hospital, Klamath Falls, Ore. May '63, 288 pp., 109 il., $11.75

☐ **TECHNOLOGICAL NEEDS FOR REDUCTION OF PATIENT DOSAGE FROM DIAGNOSTIC RADIOLOGY.** A Symposium Held Under the Auspices of the Division of Radiological Health, United States Public Health Service, Washington, D.C. Edited by Murray L. Janower, Massachusetts General Hospital, Boston, Mass. Jan. '63, 360 pp., 154 il., $6.75

☐ **CHANGING PERSPECTIVES ON THE GENETIC EFFECTS OF RADIATION** (The Beaumont Lecture for 1962) by James V. Neel, Univ. of Michigan, Ann Arbor, Mich. March '63, 112 pp., 22 il., $5.00

☐ **THE FUNDAMENTALS OF X-RAY AND RADIUM PHYSICS** (3rd Ed., 3rd Ptg.) by Joseph Selman, Univ. of Texas, Dallas, Texas. June '63, 384 pp., 306 il., $9.50

☐ **CANCER OF THE UTERUS:** From Gross Appearances to Ultrastructure (2nd Ed.) by Carlo Sirtori, National Cancer Institute, Milan, Italy, and Ettore Morano, Ospedale Maggiore, Vercelli, Italy. March '63, 408 pp., 277 il. (50 color plates) $22.50

10 Classics That Should Be in Every Roentgenologist's Library

☐ **RADIOGRAPHY OF INFANTS AND CHILDREN** by Donald B. Darling, Tufts Univ., Boston, Mass. With the technical assistance of James M. Anthony, Children's Hosp. of Pittsburgh, Pittsburgh, Pa. Dec. '62, 212 pp., 456 il., 79 tables (Amer. Lec. Roentgen Diagnosis edited by Lewis E. Etter), $16.50

☐ **IONIZING RADIATION:** An Old Hazard in a New Era by George Tievsky, George Washington Univ., Washington, D. C. March '62, 176 pp. (7 × 10), 65 il., $8.00

☐ **MODERN RADIOLOGY IN HISTORICAL PERSPECTIVE** by Stephen B. Dewing, New York Univ., New York City. Aug. '62, 200 pp., $5.75

☐ **RADIODERMATITIS** by Ervin Epstein, Univ. of Calif. Med. School, San Francisco, Calif. (With Special Chapters by Five Distinguished Contributors: Salvatore Bossio, Dell F. Dullum, Jean S. Felton, Howard Hassard, and Rees B. Rees). June '62, 200 pp., 54 il. (Amer. Lec. Dermatology edited by Arthur C. Curtis), $7.75

☐ **MEDICAL RADIOGRAPHIC TECHNIC (2nd Ed., Rev. 2nd Ptg.).** Prepared by the Technical Service X-Ray Department, General Electric Company. Under the original editorial supervision of the late Glenn W. Files. Revision by William L. Bloom, Jr., John L. Hollenbach, James A. Morgan, and John B. Thomas. June '62, 398 pp. (7 × 10), 493 il., $11.00

☐ **RADIATION THERAPY IN THE MANAGEMENT OF CANCERS OF THE ORAL CAVITY AND OROPHARYNX** by Gilbert H. Fletcher and William S. MacComb. Physics Section by Robert J. Shalek and Marilyn Stovall. All of Univ. of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas. Jan. '62, 408 pp., 346 il. (Amer. Lec. Radiation Therapy edited by Milton Friedman), $16.50

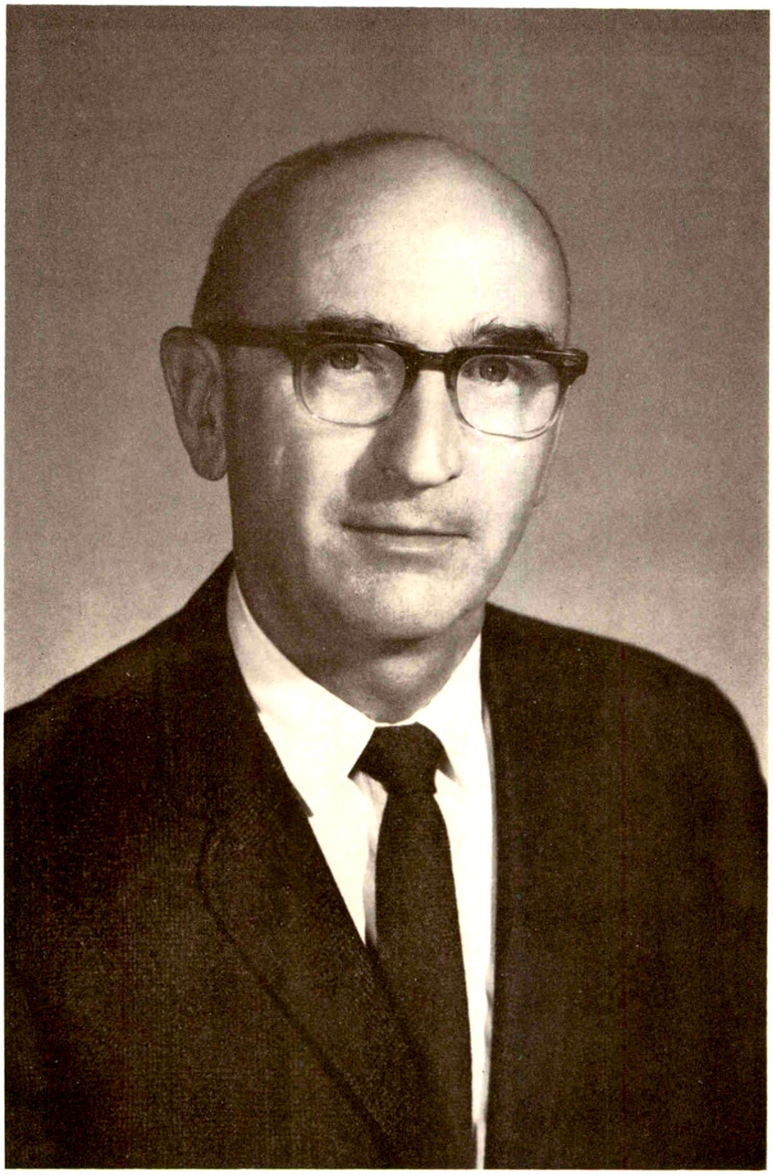
☐ **RADIOGRAPHIC ATLAS OF SKELETAL DEVELOPMENT OF THE FOOT AND ANKLE:** A Standard of Reference by Normand L. Hoerr, S. Idell Pyle and Carl C. Francis, all of Western Reserve Univ., Cleveland, Ohio. Jan. '62, 176 pp. (8½ × 11), 276 il., $9.50

☐ **THE INTERPRETATION OF TOMOGRAMS OF THE HEAD:** An Atlas by Marvin L. Daves, Univ. of Colorado, Denver, Colo., and William E. Loechel, Henry Ford Hosp., Detroit, Mich. June '62, 268 pp., 179 il. (52 in color), $17.50

☐ **THE ROENTGENOLOGICAL ASPECT OF NONPENETRATING CHEST INJURIES** by John Riley Williams and Frederick J. Bonte, both of Univ. of Texas, Dallas, Texas. Dec. '61, 148 pp., 78 il., $7.50

☐ **INTRAVENOUS CHOLANGIOGRAPHY** by Robert E. Wise, The Lahey Clinic, Boston, Mass. July '62, 160 pp. (8½ × 11), 121 il. (Amer. Lec. Roentgen Diagnosis edited by Lewis E. Etter), $9.50

CHARLES C THOMAS • PUBLISHER 301-327 East Lawrence Avenue **SPRINGFIELD • ILLINOIS**



GILBERT H. FLETCHER, M.D.

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 90 NOVEMBER, 1963 No. 5

THE PRESIDENT'S ADDRESS*

By GILBERT H. FLETCHER, M.D.
HOUSTON, TEXAS

IN THE Presidential Address, it is traditional to discuss problems of interest to the members of the Society. I have chosen to discuss the impact of biomathematics on medicine.

In the sixteenth century, the introduction of the scientific method influenced medicine only slightly. A time lag between scientific developments and their application to the practice of medicine has been, and continues to be, a consistent pattern.

Until the more recent past, medicine was essentially descriptive, because biology itself was a descriptive science. However, within a few decades, a revolution has occurred in the biological sciences. The word "revolution" is defined as a breakthrough, a basic and essential discontinuity with the past. In this instance, the discontinuity is evidenced by the transformation of biology from an essentially descriptive science to a quantitative one, similar to physics.

From its inception, physics has used mathematical formulae; progress has been made primarily through the interchange of deductions from the mathematical manipulation of models and their experimental verification. For example, almost all of the particles of matter have been predicted from the solution of equations and have then been sought in especially designed experiments.

The life sciences are similarly becoming quantitative. Models will be used more and more frequently as a research tool. In addition, increasingly complex experiments require the use of biometrics in the design of the experiments and in the interpretation of the data. Despite a time lag, quantitative methods are also being utilized more frequently in medical research.

There is an awareness that men who are ungrounded in mathematics will be increasingly limited in their grasp of the main forces of civilization. In several colleges, courses in mathematics are now offered not only to those who specialize in mathematics, but also to those who are preparing for careers in the social sciences, business, finance, or medicine. Such training is now essential in order to render these graduates sufficiently literate in mathematics to keep abreast of modern trends. Courses in those aspects of mathematics that are essential to the understanding of modern biology and medicine should be included in radiotherapy training programs.

---

* Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963.

There have been two milestones in the revolution of information processing. The first of these was the publication in 1925 of Sir Ronald Fisher's book "Statistical Methods for Research Workers." The second was the development of automatic computers in the 1940's. Both of these developments are bringing to our civilization a revolution, the impact of which is inconceivable and can be compared to the impact of the technological revolution.

Before the publication of Sir Ronald Fisher's book, the theory of probability had been almost entirely a hobby of mathematicians. It was not until statistical methods were made available that a wide range of applications for this theory was found in the biological sciences, agriculture, technology, manufacturing, and merchandising. World War II provided a tremendous impetus to the use of statistics, which has now been extended to all fields of human productivity. The concept of statistical decision has revolutionized man's most important attribute, "decision-making," by transfering its basis from intuition to a very efficient scientific method.

Clinicians usually make decisions for a particular patient in the light of their own experience on a background of data provided by the medical literature which may not have adequate statistical significance. However, there is an increasing awareness in current medical publications that the number of cases in the reported series are small or that the series are not quite comparable. Statistical significance is given to differences observed and many clinical investigations are using biometrical designs.

The impact of biometrics upon medicine should change the attitude of the clinician in his actual management of patients. In deciding what is best for the individual patient, he should make his decision on a scientific basis. When noncontroversial data to help him choose the best definitive therapy do not exist, the clinician should be impelled to find objective answers.

Computers are solving problems and answering questions which were previously beyond the practical capacity of the human mind to solve or answer. The industrial revolution added the power of inanimate energy to that of the muscles of men and animals. The inanimate power of the new automatic computers augments enormously the brain of man. It is no overstatement to say that the impact of automatic computers is beyond human comprehension.

Computer techniques have not yet been widely used in clinical medicine. However, these techniques have made possible the extensive use of statistical methods and time-consuming explicit calculations in the planning of external beam and interstitial gamma-ray therapy. Constant physiological monitoring is being developed as an investigative instrument.

Making available correlations which would be too tedious to obtain by paper and pencil manipulation, the coding of clinical data on punch cards has been a definite step forward. However, the punch card system is a rudimentary tool compared to the recording of information on magnetic tape. What is designated as "information retrieval" will produce changes in the handling of clinical data; we cannot grasp the significance of these changes, just as physicists 30 years ago could not visualize the problems that are now solved without difficulty.

The composition of the membership of the American Radium Society makes it, among medical societies, one of the best equipped to meet the changes wrought by these new technologies. Among our members we have physicists and radiobiologists who, by their training and scientific pursuit, are quantitatively minded. The radiotherapists who routinely use geometric techniques and elementary mathematical formulae can also be made cognizant of biomathematics and computer methods.

Furthermore, the membership is composed of representatives of several medical disciplines. We have surgeons, internists, and radiotherapists, all of whom are interested in the definitive treatment of cancer patients with measurable end results. In many clinical situations, surgery, radiotherapy, or chemotherapy are competitive modalities of treatment. In other situations, these methods can be used alone or in combination; they offer opportunities for biometrically designed clinical experiments.

Toynbee has based his explanation of the natural history of civilization upon the response to a challenge. The present challenge facing clinical medicine is to integrate scientific methods without losing the fundamental doctor-patient relationship. At times there is, I believe, almost purposeful confusion in the statement that it is irreconcilable to practice the art of medicine scientifically. Cancer therapy should be a blend of individual clinical experience, which cannot be replaced, with the scientific value of that particular experience rather than with its semimystical decision-making component.

Our programs should reflect the impact of newer methods. By making the audience aware of developments of intense interest in biomathematics and computer technology, our society will actively help to keep medicine abreast of the scientific advances taking place in the life sciences.

The University of Texas
M. D. Anderson Hospital and
Tumor Institute
Houston 25, Texas

PRIMARY PROCESSES OF DEPOSITION OF RADIANT ENERGY AND INITIAL RADIOCHEMICAL EVENTS*

By JOHN W. BOAG
NORTHWOOD, ENGLAND

THE biological effects of ionizing radiation are the end result of a complex chain of processes which begins with the initial transfer of energy from the primary radiation to the molecules of the irradiated material. This energy may then pass through the form of molecular ionization or excitation, dissociation and radical formation, before it is finally degraded to heat or to permanent chemical change. One feature common to all the links in the chain is the discrete nature of the processes involved. This is true not only of the initial physical interaction between a photon or a secondary electron and a molecule, but even of the final step which determines the biological damage, since the cell, too, is a discrete unit, whose structure or function can be damaged by a very small amount of energy delivered in an appropriate form at a suitable place.

It was recognized by the earliest workers in the field that this discreteness of action was the clue to the extraordinarily high effectiveness of ionizing radiation in terms of biological damage per unit of energy absorbed. This conclusion remains true today, and a thorough understanding of the initial molecular events, of the chemical species formed, and of the subcellular lesions is essential if we are to replace the crude but very fertile target theory of earlier days by a more detailed and rational theory of radiation action

The task I have been set . . . is to review the primary physical and physicochemical processes which come first in the time-sequence of events, and especially to draw attention to any new experimental or theoretical discoveries which may have modified our view of this part of the field during the past few years. To do this and, at the same time, maintain a balanced view of the whole field is not easy. The balanced view changes only slowly from year to year, and we do not yet know whether the changes in the picture which are demanded by recent discoveries will be far-reaching or possibly only trivial in their practical consequences. These new facts are, however, at the present time the growing points in this branch of the subject, and as such they are likely to be of more interest than a recapitulation of familiar material would be.

There are some salient facts about the interaction of radiation with matter which need not be discussed at length but which it is useful to set down explicitly, as they may be considered to be the axioms of our subject in its present state of development.

1. The chemical and biological changes observed are initiated by the energy deposited in the material.

2. This energy is distributed through the material by the interaction of fast charged particles with the molecules of the medium. When the primary radiation consists of quanta or uncharged particles, these first transfer kinetic energy in their collisions with molecules, and the secondary charged particles which emerge from these collisions then distribute this energy through the material.

3. The charged particles transfer their energy by ionizing and exciting some of the molecules in the vicinity of their tracks.

4. The ionized or excited molecules and the ejected electrons may retain their identity for a brief interval, but they then undergo a variety of transformations, some of which lead to new stable molecules and others to reactive molecular fragments (radicals, excited atoms, etc.).

5. The reactive chemical species are pro-

---

* Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963. Part of the Symposium: The Fundamentals of Radiobiology; Chairman, Dr. Henry S. Kaplan, Palo Alto, California.

duced along the tracks of the secondary particles, a proportion of them being in clusters of high local concentration. They may, therefore, undergo reactions among themselves (recombination, dimerization, etc.) before diffusing further afield.

6. Molecules or structures of vital importance to the cell may be damaged either by direct transfer of energy to them from a charged particle, leading to ionization, excitation or bond breakage within some part of their structure, followed by dissociation or other chemical change, or they may be attacked by the reactive chemical species formed by the radiation in their vicinity.

These axioms are illustrated diagrammatically in Figure 1 which shows at the top the primary collisions leading to ejection of secondary charged particles. An enlarged view of the structure of a secondary particle track is shown beneath this, ionized and excited molecules being represented by dots and crosses respectively. An enlarged view of a single segment of this track—a cluster, or "spur" as it is called by radiation chemists—is then shown, at a time some 10^{-10} seconds after the passage of this particle, when the ionized or excited species have mostly been converted (by dissociation or reaction with their neighbors) into radicals, although some of the primary species still remain. In a time ranging from microseconds to milliseconds, these radicals will then react with some of the biological molecules marked M. In addition, of course, some of the biological molecules may have been damaged by direct interaction with the primary radiation.

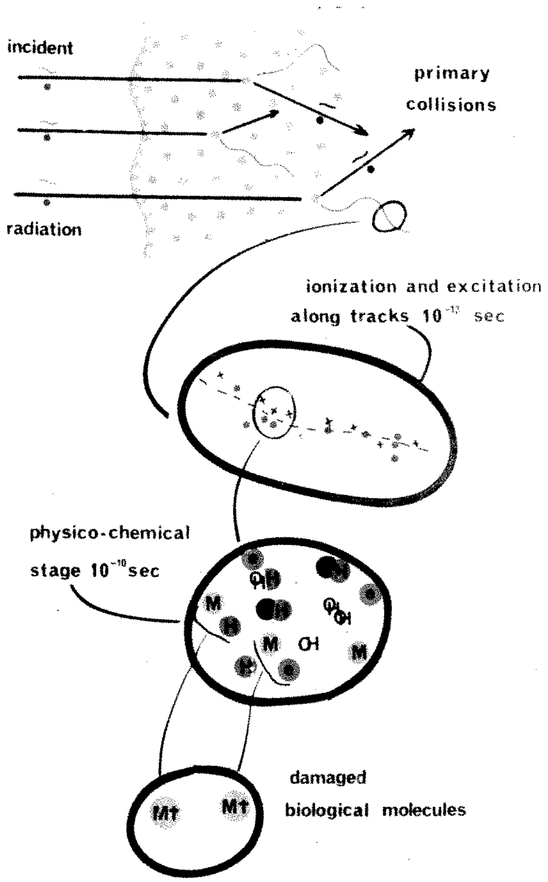


Fig. 1. Diagrammatic representation of the physico-chemical and chemical stages in the transfer of energy from ionizing radiation to biological molecules.

The axioms which are stated above in rather general terms would not excite serious controversy. Immediately one enters into finer details, however, and asks what species are produced and how they interact—at this point one is on controversial ground. Hitherto such discussions have had to be conducted largely on theoretical principles, but improved experimental methods are now opening up the field to direct observation and measurement. The first new data which I wish to discuss are, however, of a theoretical nature. Platzman[23–27] has shown that the attempt to follow through the physical and physico-chemical processes in a theoretically satisfactory manner can be extremely fruitful, and many of the new facts I shall be reporting come directly from his theoretical work, or from experiments stimulated and interpreted by his ideas.

The conventional picture of a charged-particle track which is illustrated in Figure 1 is based directly on cloud-chamber photographs of electron tracks or α-particle tracks in a gas. In gases the separate ions act as condensation nuclei for the vapor present, and their number can be counted on the photographs in the case of electron tracks, or determined by charge collection methods for α-particles. It is not always realized that the balance between ionization and excitation may be quite different in a liquid or a solid medium from that which obtains in a gas, and until reliable experimental evidence on this point is available, we must regard quantitative deductions based on the conventional model of a track as somewhat speculative.

It has generally been assumed that the excited molecules along the track of a charged particle were simply those which had received a small energy transfer, insufficient for ionization, and that any molecules which received an energy transfer larger than the binding energy of the most loosely bound electron would be ionized forthwith. This has recently been shown by Platzman to be incorrect.[25,26] When a charged particle interacts with a molecule, there is an appreciable probability that the latter will be left temporarily in an excited state, the energy of which exceeds that required for ionization. The molecule may, of course, get rid of its excess energy by ejecting an electron and thus becoming ionized, but the practical importance of Platzman's findings is that such a "super-excited" molecule may find other ways of divesting itself of the excess energy, ways which do not involve ionization. It may, for instance, dissociate into two radical fragments. These may be liberated with considerable kinetic energy, and either or both of them may be in an excited state. In any of these processes, reactive chemical species are produced without the energy passing through the stage of ionization.

The probability of excitation to different energies has been calculated by Platzman[26] for a number of simple molecules, and calculations for others are in progress. The calculations make use of very varied experimental data, ranging from optical absorption coefficients to the ionization cross section for fast charged particles and the mean energy required to form an ion pair. The excitation spectrum for methane is shown in Figure 2. It is very clear that the strongly excited states all lie far beyond the visible and near ultra violet region of the spectrum which is represented by the tiny peak at the left hand corner of the graph. The most probable excitation energy lies close to the

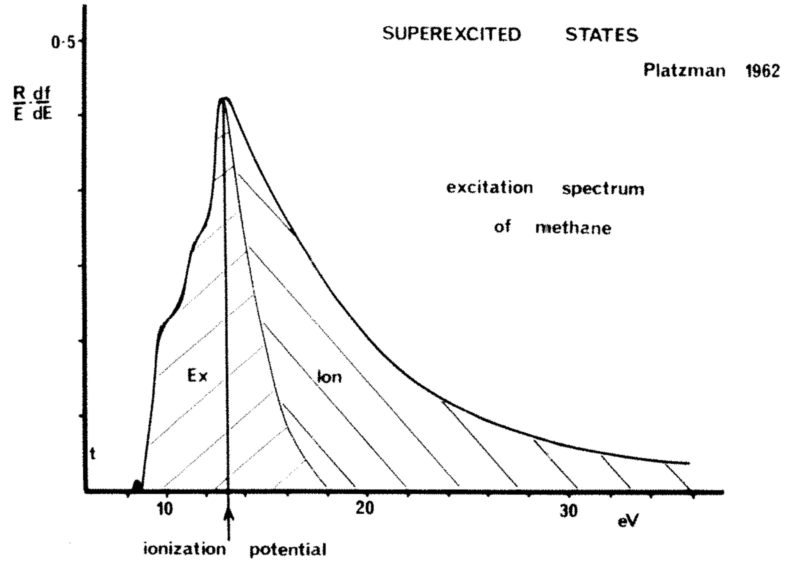


FIG. 2. Probability of energy transfer from a fast charged particle to a molecule of methane as a function of the amount of energy transferred. The balance between excitation and ionization is indicated by the two shaded areas under the curve.

ionization potential at about 13 ev. Platzman's estimate of the proportion of those "superexcited states" lying above the ionization potential which do not lead to ionization is represented by the shaded area under the curve to the right of the ionization potential, although the incomplete nature of the experimental data renders this estimate somewhat uncertain. In addition to demonstrating the unexpected finding that excited states lying above the ionization potential have a real existence, the curve shows that among the more normal excited molecules there is a great preponderance of high-energy states over low-energy states. These highly excited states, even though they lie well below the ionization potential, would nevertheless cause dissociation or multiple bond breakage in the affected molecule.

In the past the relative importance of ionization and excitation in radiobiology has sometimes been assessed by comparing the high efficiency of ionizing radiation in producing a particular biological effect with the much lower efficiency of ultra violet radiation having a quantum energy of some 5 ev. (2,537 Å) which is able to excite but not to ionize. It is implicit in such a comparison that the most probable excited states produced by ionizing radiation are identical with those produced by ultraviolet radiation, and this assumption is now seen to be incorrect.

The relative importance of excitation and ionization cannot easily be settled by direct experiment, however, as this would involve working with vacuum ultra violet radiation and radiation of this wave length is too strongly absorbed to permit the conventional external irradiation techniques to be used, even on objects as small as single cells. Indeed, we have to recognize that so-called ionizing radiation, acting by way of the secondary charged particles liberated throughout the irradiated object, is also a much more efficient exciting agent than any ultra violet radiation which it is practicable to use and is indeed the only means of inducing such highly-excited molecules at appreciable depths within an object. The greater biological effectiveness of ionizing radiation is, therefore, not necessarily due to the ionization produced. It may rather depend upon the fact that *nearly all* the energy deposited by ionizing particles is communicated to molecules in much larger "packets" than is the energy deposited by conventional ultra violet radiation.

Another question which has excited controversy is the fate of the free electron ejected from an ionized molecule. Is it usually bound by the Coulomb field of the parent ion, to return and recombine with it, as maintained by Magee,[19] or is it more frequently stabilized or captured in some way by other relatively distant molecules, in accordance with the Lea,[18] Gray, and Platzman[23] hypothesis? There is some recent experimental evidence bearing on this question.

Ten years ago Platzman[24] pointed out that on energetic grounds a free electron was incapable of carrying out the reaction with a water molecule which had frequently been prescribed for it by radiation chemists. The electron must first become "solvated" before the energy requirements of the reaction could be met. He predicted that such solvated electrons, which in aqueous media he called "hydrated electrons," should exhibit certain characteristic physical properties, and might live long enough to be detected and to react chemically in unusual ways.

During the past 5 years, evidence has accumulated of the existence in irradiated aqueous solutions of a reducing species which could diffuse much more rapidly than the hydrogen atom and which reacted somewhat differently.[2,20] This unusually mobile species has been shown to possess a negative charge,[6,7] and the presumption has been that it must be an electron loosely bound, in some way not precisely understood. Recently, a transient optical absorption spectrum has been found in irradiated water, the form of which strongly supports the view that the fugitive species is Platzman's "hydrated electron."[13] In order to understand the phenomenon of "solvation," we must look at an exactly similar case involving nonbiological molecules.

It has been known for many years that when sodium metal was dissolved in liquid ammonia, the sodium atoms dissociated into ions and electrons. These electrons became solvated in the polar liquid and retained an independent existence almost indefinitely.

Platzman and Franck[27] pointed out in 1954 that a theory of the optical properties of such solutions could be worked out in a manner similar to the theory which they formed for halide ions in solution. Independently, a similar approach was made in 1954 by Deigen,[9] in Russia, based on a suggestion by Davidov[8] in 1948. A simple, but necessarily inexact, explanation of the solvation state of the electron is the following:

When an electron has been slowed down to thermal energy in any highly polar liquid whose molecules cannot readily capture electrons, it is to be expected that the liquid molecules surrounding the electron will tend to align themselves in the electric field of the latter, as shown in Figure 3. Thermal motion will prevent persistent polarization of the molecules immediately adjacent to the electron, but the polarization further out, although weaker, will be more extensive and more persistent. If we imagine the electron itself to be instantaneously removed from its central position in this assemblage but the molecular polarization to be "frozen in," we can see that a positive potential well must exist. In this well, which it has dug for itself, the negative electron is trapped almost as effectively as if it were bound to a positively charged nucleus. A quasi-molecule is formed in which the electron is bound not to one but to an assemblage of many water molecules, and according to quantum theory the electron can occupy only certain prescribed orbits in this field—it has quantized energy levels. Transitions between these energy levels give rise to the optical absorption spectrum.

In order to observe the electron solvated in water Hart and Boag[13] employed the technique of absorption spectroscopy in the wave length region between 2,000 Å and 9,000 Å; *i.e.*, in the ultra violet, visible and near-infrared regions. The experimental ar-

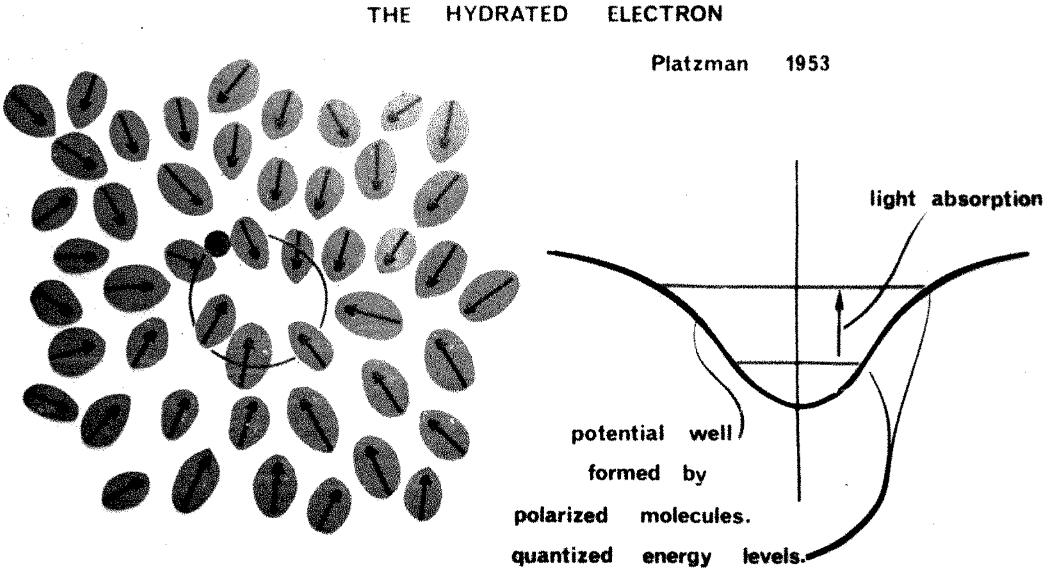


Fig. 3. Diagrammatic representation of the polarization induced in water by a self-trapped, or "hydrated," electron.

rangements are illustrated in Figure 4. The electron pulse was fired into the solution, and after a predetermined delay the absorption spectrum of any transient species present was photographed by triggering a spark light source. The resolution of the experimental set-up was limited by the duration of the light flash, which lasted some 5 microseconds.

Figure 5 shows a spectrogram taken through pure, de-aerated water exposed to a 2 microsecond pulse of 1.8 mev. electrons. The upper of the three spectra illustrated was taken through the water before irradiation, and shows the spectral distribution of the spark light source used in the experiments. The middle spectrogram was taken simultaneously with the 2 microsecond electron pulse, and the third one some 30 seconds later. The transient absorption band which is present in the simultaneous spectrogram is more clearly seen from the optical density difference based on densitometer traces of the spectra. This difference curve is shown in the upper part of Figure 5. It has a peak at 7,000 Å and a long tail extending through the visible and the ultra violet regions. A spectrum consistent with this has also been found by Keene[16] in the wave length region below 6,000 Å. Figure 6 shows the absorption spectrum of the hydrated electron at the top and the absorption spectrum of the electron solvated in ammonia below (on a displaced wave length scale).[11] The similarity in form is apparent.

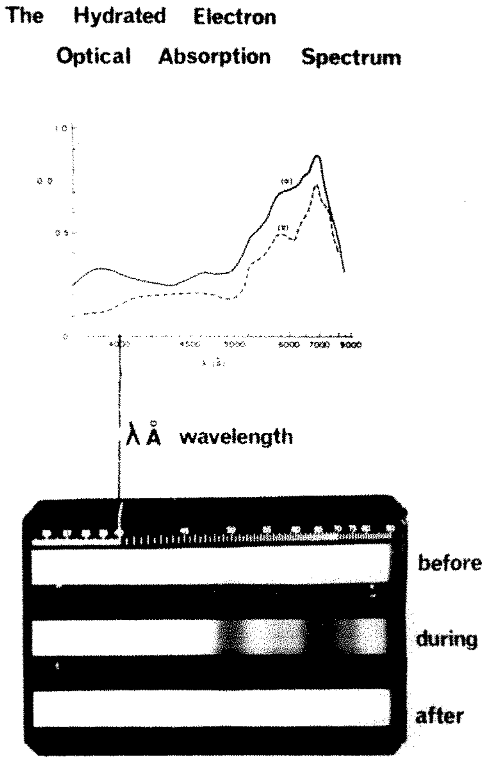


Fig. 5. The optical absorption spectrum of the hydrated electron. *Above:* The optical density difference curves derived from the spectrogram. (a) 0.5 M sodium carbonate solution de-aerated. (b) Pure neutral water de-aerated. (Reproduced from *The Journal of the American Chemical Society.*) *Below:* An absorption spectrogram showing the absorption which occurs during irradiation. (Reproduced by permission from *Argonne News.*)

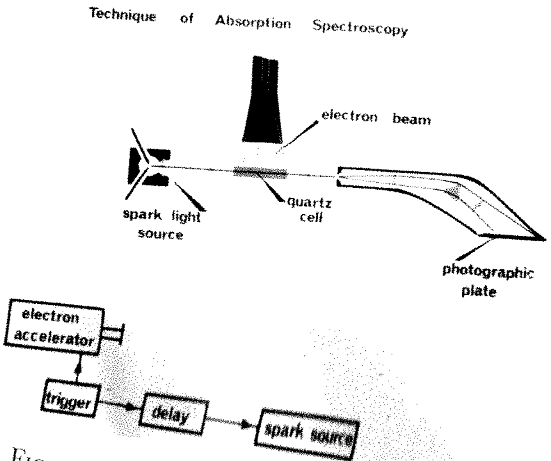


Fig. 4. Apparatus used for kinetic absorption spectroscopy.

The electrons solvated in liquid ammonia not only have a characteristic absorption spectrum, but also produce high electrical conductivity in the solution.[15] Further evidence that the transient absorption spectrum in water is due to the hydrated electron has now been provided by conductivity measurements carried out immediately after a pulse of fast-electron radiation.[3] These measurements, which will be described in full elsewhere, showed a transient conductivity which decayed at

same rate as

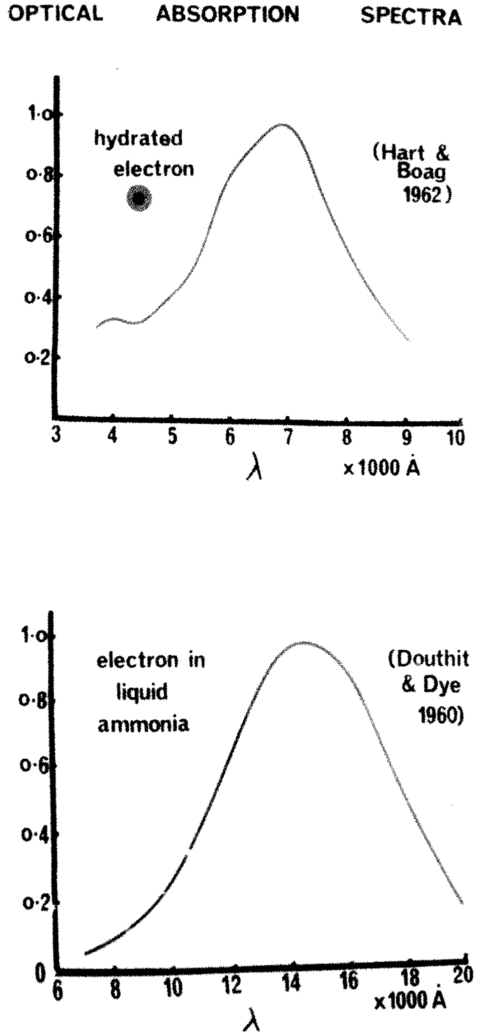
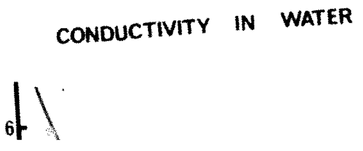


Fig. 6. Comparison of the optical absorption spectra of the hydrated electron and of the electron solvated in liquid ammonia.

served in oxygenated water is shown in Figure 8.[4] At a dose per pulse of 15 kilorads, this absorbing species decayed to half its initial intensity in some 400 microseconds. It is believed to be the O_2ion, and conductivity measurements in oxygenated water indicate that the decay follows second order kinetics.

Another electron scavenger—benzophenone—which was suggested by Baxendale[1] for a radiation-chemical experiment—has recently been proposed by Adams and tested by Dewey and Adams[10] as a sensitizer in a radiobiological experiment using bacteria. The results are shown in Figure 9. The sensitivity of the bacteria is considerably higher in the presence of benzophenone than in pure nitrogen, but not as high as when oxygen or NEM is present. Other fruitful suggestions of this kind may follow from a better understanding of the primary species which are formed. Kinetic absorption spectroscopy has already yielded many other interesting results in radiation chemistry and its application to biological molecules will not be long delayed.

Another physical method of studying the unstable species formed by irradiation is electron spin resonance (ESR) spectroscopy. This technique enables one to detect



BIOCHEMICAL BASIS OF REPRODUCTIVE DEATH IN IRRADIATED CELLS*

HENRY S. KAPLAN, M.D.
PALO ALTO, CALIFORNIA

IONIZING radiations in sufficiently high doses can break almost any chemical bond.[21] A truly comprehensive discussion of radiation biochemistry would therefore be almost unlimited in scope. In this symposium, we are primarily interested in the killing of cells by ionizing radiations. We know that radiation causes an unusual kind of cell death, characterized by the loss of reproductive integrity, *i.e.*, of the capacity for sustained cell division. It seems desirable, therefore, to focus our attention on the initial biochemical lesions induced by ionizing radiation which might cause this loss of reproductive integrity.

The spectacular unfolding of molecular biology in the past two decades has given us a much clearer picture of the roles played by the various kinds of macromolecules in the cell.[3] Virtually all of the actual work performed by the cell (metabolism, secretion, contraction, etc.) is carried out by its enzymes and other proteins. The remarkable specificity of action of each protein has been shown to be due to the sequential assembly order of its component amino acids. Since the function of a protein may be lost or altered by a change in even a single amino acid, nature must have evolved a remarkably error-free mechanism for the synthesis of proteins. This has been accomplished by coding the information which governs amino acid sequence in the form of another sequence; namely, that of the purine and pyrimidine bases of the nucleic acids. In these macromolecules, hundreds of nucleosides, each containing a purine or pyrimidine base and a pentose sugar, are linked by a phosphate ester backbone to form long chains or strands. There are two general classes of nucleic acids: deoxyribonucleic acid (DNA), in which the pentose sugar is deoxyribose; and ribonucleic acid (RNA), in which it is ribose. DNA is confined to the chromosomes of the cell nucleus, whereas RNA occurs in both the cytoplasm and the nucleus and is particularly abundant in the nucleolus. The master code is carried by the DNA, the structure of which must therefore be such as to guarantee the exact and unvarying duplication of each DNA molecule, in addition to providing the information which governs the synthesis of proteins. The actual function of overseeing the synthesis of proteins is, however, assigned to RNA. The term "*messenger RNA*" has recently been coined to refer to the class of RNA molecules which are synthesized directly on the chromosomal DNA and have a corresponding purine and pyrimidine base sequence, which represents a kind of "transcription" of the genetic code of DNA.[11,19,33] The messenger RNA molecules carry the translated code to the actual protein assembly sites, the cytoplasmic ribosomes, which are composed in large part of high molecular weight *ribosomal* RNA. The function of transporting the amino acids to the same assembly point is performed by a third class of RNA, of relatively low molecular weight, known as *transfer* or *amino acid-acceptor* RNA.

Although RNA and protein are synthesized almost continuously throughout the cell-division cycle with a transient pause during the actual process of mitosis, DNA is duplicated only during a discrete period of time (the DNA-synthetic or S phase, occurring during interphase) prior to each

---

* Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963. Part of the Symposium: The Fundamentals of Radiobiology; Chairman, Dr. Henry S. Kaplan, Palo Alto, California.

Certain studies cited herein were supported by grants C-6437 and C-2896 from the National Cancer Institute, National Institutes of Health. Dr. Kendric C. Smith made numerous helpful suggestions during the preparation of this manuscript.

cell division. Doubling of the cell's complement of DNA is followed in prophase by progressive condensation and duplication of the chromosomes, which line up in the mitotic spindle during metaphase and separate during anaphase to provide identical DNA complements to each of the daughter cells.

In the Watson-Crick[62] model of DNA structure, the macromolecule is composed of two long intertwined polynucleotide strands in which each successive purine or pyrimidine base is linked by hydrogen bonds to a specific pyrimidine or purine, respectively (adenine pairs with thymine, guanine with cytosine). The two strands are believed to come apart during the process of synthesis of new DNA. Each "old" strand can then serve as a template for the synthesis of a new strand, resulting in two double strands, each half old and half new. The sequence of purine and pyrimidine bases in each newly synthesized strand is determined by obligatory pairing with each preexisting base in the old chain. It is this feature of complementarity in the purine-pyrimidine base relationships along the two chains of DNA which enables the synthesis of such a huge and complex macromolecule to remain so remarkably error-free.

INVESTIGATIVE APPROACHES IN RADIATION BIOCHEMISTRY

The random distribution of ionizing events and the low atomic number of living systems make it extremely improbable that any one class of molecule will suffer selective injury. Most of the ionizations in a cell are believed to occur in water, producing highly reactive but short-lived free radicals which may recombine harmlessly to yield water again or may interact with nearby macromolecules, usually causing chemical bond breakage. The destruction of one or two molecules of a particular substance might or might not have serious consequences for the cell, therefore, depending on: (a) the number of intact molecules of that substance which remain; and (b) the capacity of the cell to repair the damaged molecules or to replace them with new ones. Present evidence suggests that, although there may be many molecules of DNA in a cell, there will be very few (perhaps only one) with any particular base sequence. Since such a unique molecule is also the template for its own replication, damage to it might well be irreparable, and its loss might in turn be fatal for the cell. In contrast, damage to messenger RNA would readily be repaired by synthesis of new molecules on the corresponding DNA template. Damage to the other classes of RNA molecules or to protein is even more unlikely to have dire consequences, since these are relatively abundant and can, in any case, be readily replenished. By this inductive process, therefore, one might well anticipate that DNA would prove to be the "Achilles heel" of cells exposed to ionizing radiation.

Let us now examine the available evidence. Most studies of the biochemical effects of radiation have employed either a *chemical* or an *analytic* approach. In the chemical approach, the biochemical entity selected for investigation is extracted and purified, irradiated *in vitro* in the wet or dry state, and then compared with an unirradiated sample with respect to some change in its physical properties (viscosity, sedimentation constant, light scattering, spectral change) or its chemical properties or behavior (release of inorganic phosphate groups, loss of antigenicity or enzymatic activity, appearance of abnormal radioproducts, etc.). This method permits the quantitative estimation of radiochemical yields for a great variety of substances after exposure to radiations of different LET. Moreover, where two or more radiochemical reactions occur in the same substance, it enables an appraisal of their relative importance, at least under *in vitro* conditions, to be made. However, these chemical advantages are offset by the severely limited biologic applicability of such data. Detection of significant changes in physical or chemical properties requires the radiochemical alteration of a substantial fraction of the molecules of the test substance, necessitating the use of enormous radiation doses, far beyond the biologic range. Moreover, extraction and purification of the macromolecular components of cells or tissues may subject them, if only briefly, to enzymatic degradation, to shearing forces during centrifugation, and to other deleterious conditions which may produce significant alteration from the native state. The radiation response of such altered macromolecules could not be expected to mirror accurately their radiochemical behavior *in vivo*. Such considerations make it obvious that the chemical approach, though very useful in certain respects, cannot provide a definitive answer to the central question we have posed here.

In the analytic approach, cells or tissues are irradiated with a fixed dose or with a graded series of doses and are then analyzed for their content of a particular molecule or for the activity of a particular enzyme at some arbitrary time interval or at a series of time intervals thereafter. Here again, as in the chemical approach, a substantial fraction of the molecules of the test substance must be altered to detect any change. If a change is observed, how can one decide whether it is indeed due to primary events (ionizations or free-radical interactions) or merely one of many possible secondary biochemical disturbances in a damaged cell? If the tissue under study is composed of two or more cell types which differ in the enzymatic activity or other biochemical indicator chosen for analysis, can one exclude spurious changes due to differential killing of one of these cell types? The latter problem can be mitigated by working with relatively homogeneous tissues or with cell cultures *in vitro* and by studying biochemical phenomena which occur too soon after irradiation to be accounted for by cell death. Nonetheless, the analytic approach remains subject to the disadvantage that the biochemical disturbances measured have no necessary relevance to the reproductive fate of the cell.

More recently a *molecular biologic* approach has been employed. A selective aberration is introduced into one class of molecule in a cell population, which is then irradiated with a graded series of doses and assayed for cell viability by methods which measure the reproductive integrity of individual cells. Biochemically unaltered control cells are simultaneously irradiated and tested for viability. The slope of the exponential portion of the dose-log survival curve is a convenient index of radiosensitivity. It is reasonable to postulate that chemical pretreatments which significantly alter this slope must interact with some biochemical system or moiety which plays an essential role in cytocidal radiation injury. If the chemical pretreatment employed is known to interact with only one class of molecule in the cell, its ability to alter radiosensitivity would strongly implicate that class of macromolecule as a primary target of lethal radiation effect. Correlative studies which do not involve chemical pretreatment may also yield selective evidence of this kind.

ALTERATION OF THE PHYSICAL AND CHEMICAL PROPERTIES OF BIOCHEMICAL SUBSTANCES IRRADIATED IN VITRO

Solutions of DNA irradiated *in vitro* suffer a decrease in viscosity, attributed to scission of the sugar-phosphate backbone of both strands, yielding fragments of reduced length.[12] Chain breakage also occurs in irradiated RNA, with a concomitant change in ultracentrifuge sedimentation behavior.[65] Cross-linking has been invoked by Alexander and his associates[2,40] to explain anomalous solubility behavior in irradiated DNA and may constitute a second type of radiation effect on DNA structure. Still another molecular mechanism, presumably related to radiochemical attack on the pyrimidine and/or purine bases, seems implicated by the reported decrease in melting temperature[41] of irradiated DNA at doses over 10,000 r.[6] Extracted deoxyribonucleoprotein (DNP) has been reported to be much more sensitive than free DNA to radiation-induced loss of viscosity,[7,17] at least under conditions in which the indirect effects of radiation were operative. However, such observations may well be due to the inevitable presence of nucleases and other enzymes in these preparations.

Chemical studies of irradiated RNA and DNA[48,49] suggest that radiochemical attack occurs preferentially on the purine and pyrimidine bases. Concomitant with loss of viscosity, the damaged macromolecules liberate titratable acid groups, inorganic phosphate, ammonia, altered nucleosides, and free purines. Ammonia formation appears to be distinctly oxygen-dependent, whereas inorganic phosphate liberation is not.[50] Several radiochemical mechanisms have been invoked to explain these observations: (a) deamination and ring opening of the bases; (b) cleavage of the purine glycoside linkages, liberating free purines; and (c) cleavage of phosphate ester bonds, liberating inorganic phosphate and titratable acid groups.

When the free bases are irradiated in solution, the pyrimidines lose their ultraviolet absorption due to attack on the double bond between carbons 5 and 6. Unstable intermediates, involving water addition at these sites, may progress to form stable hydroperoxide or glycol derivatives.[16,51] In the purine nucleosides, cleavage of the C_8N_9 bond results in opening of the imidazole ring; in the presence of oxygen, the glycoside linkage then becomes labile, with release of the altered base and unaltered free pentose.[23,24]

Much less is known about the effects of irradiation *in vitro* on protein structure. Changes in sedimentation and solubility behavior have been observed, with a concomitant increase in number of disulfide bonds.[1,47] No evidence for scission of the main polypeptide chains could be detected.

EVIDENCE DERIVED FROM BIOCHEMICAL ANALYSIS

Radiobiochemical investigations have been quantitatively impressive, though beset by numerous pitfalls, as already mentioned. Since extensive and detailed reviews are available,[45] the treatment presented here has been deliberately selective.

Reproductive death of irradiated cells is compatible with the maintenance of normal rates of respiration, carbohydrate metabolism, and synthesis of protein and RNA.[26,27] Assays of the activity of a great variety of enzymes extracted from irradiated tissues have indicated increased activity in some instances, no change in others, and decreased activity in still others. Since many of these investigations were performed under conditions in which selective cell death probably occurred, such changes in activity may simply reflect a shift in cell population in the irradiated tissue. It seems advisable to restrict the discussion to those analyses which, by virtue of having been made at relatively early time intervals after irradiation at doses in or near the biologic range, give somewhat greater promise of being relevant to the phenomenon of reproductive death. Application of these criteria eliminates all but the following observations: (a) decreased oxidative phosphorylation; (b) decreased activity of certain intranuclear and induced enzymes; and (c) inhibition of DNA synthesis.

Uncoupling of oxidative phosphorylation in spleen and thymus homogenates and mitochondrial fractions, after exposure to several hundred r, has been known for some years. Detailed investigations by Van Bekkum[59] reveal that this phenomenon could be detected as early as 2 hours after irradiation of spleen or thymus, that doses as low as 50 r were effective in thymus, and that no such effect occurred in mitochondrial preparations from normal or regenerating liver treated with much higher doses. Spleen mitochondria irradiated *in vitro* with doses up to 20,000 r failed to exhibit this response. Since pyknotic changes can be detected within 1 to 2 hours in the nuclei of irradiated spleen and thymus cells, there is no compelling reason to ascribe cell death in these radiosensitive tissues to a primary mitochondrial lesion.

Several years ago, ATP-generating enzymatic activity was noted in isolated nuclei prepared from calf thymus.[46] Similar nucleoside triphosphate kinase activity was later reported in nuclei from rat spleen, thymus, bone marrow, lymph nodes, and intestine, but not from liver, pancreas, kidney, or brain. Irradiation of the radiosensitive tissues with doses as low as 25 r sharply inhibited this kinase activity; inhibition was detectable within a few minutes after treatment.[13] Although the early occurrence and great radiosensitivity of this phenomenon are of interest, there is no evidence as yet to establish it as a primary event leading to cell death in these sensitive tissues. Instead, newer knowledge concerning DNA and nuclear RNA synthesis provides a plausible interpretation for the phenomenon in terms of radiation damage to DNA, rather than to the enzyme protein itself. The enzyme DNA polymerase synthesizes DNA from its four nucleoside triphosphate precursors in the presence of pre-existing DNA, acting as a template or primer.[8,10] Nuclear RNA has now been shown to be synthesized by another enzyme, designated RNA polymerase, which again requires DNA as a template for the assembly of the four ribonucleoside triphosphates.[32,55,63] It is not unlikely that nucleoside triphosphate kinase activity, through "feedback" mechanisms, is closely keyed to the activity of RNA polymerase. Primary radiation injury to DNA, by interfering with its primer function for RNA polymerase, might well lead to secondary physiologic inhibition of kinase activity. Novelli and his associates[43] have provided direct evidence in support of such an interpretation in another biochemical system. Roentgen irradiation of *E. coli* inhibited the induced synthesis of the enzyme β-galactosidase, and cell-free extracts from irradiated cells exhibited no activity unless supplemented with intact DNA prepared from cells containing the gene for β-galactosidase synthesis. These results have been interpreted in the light of modern concepts of the role of messenger RNA in protein synthesis: Irradiated DNA *in vivo* is apparently unable to function as the template for messenger RNA synthesis, and β-galactosidase cannot be synthesized for lack of its specific messenger RNA.

Finally, we may examine the significance of the observation that DNA synthesis measured in terms of the incorporation of radioactive precursors is partially inhibited in irradiated tissues. This response, originally noted by Hevesy,[25] has been confirmed and extended by many other workers.[29,45] However, the interpretation of such data has probably been the subject of more effort and controversy than have gone into all other radiobiochemical studies combined. Since DNA doubling must occur prior to each mitosis, it was natural for the early investigators to suppose that the inhibition of DNA synthesis offered a biochemical explanation for radiation-induced mitotic arrest. However, more careful analysis of the timing of DNA synthesis and of the radiosensitive and insensitive stages of the mitotic cycle has placed this work in a quite different perspective.[29,30,57,64] It now appears that the synthesis of DNA is not a highly radiosensitive process and that most, or perhaps all, of the observed effect is the consequence rather than the cause of mitotic inhibition.

It should be stressed that it is the synthesis of the entire cellular complement of DNA that is measured in such studies. If radiation were to cause lesions in one or a very few of the many different molecules of DNA in the cell, the inability of the lesioned molecules to perform their functions, including that of cell-replication, would escape detection by presently available biochemical methods, though readily revealed in the genetic and reproductive behavior of the cell.

EVIDENCE DERIVED FROM STUDIES UTILIZING THE MOLECULAR BIOLOGIC APPROACH

Powerful new tools were provided for the radiobiologist with the synthesis of a series of analogues of the natural purine and pyrimidine bases. These compounds, which are identical to the corresponding natural base except for one abnormal substituent, were originally exploited as metabolic antagonists, and some of them have found a useful role in cancer chemotherapy. However, during the past 10 years, it has been observed that certain of these analogues, under favorable conditions, may become incorporated into nucleic acids by substituting for the corresponding natural base.[15,28,61] Their incorporation results in "fraudulent" nucleic acid molecules, the properties of which have been shown in some instances to be significantly altered.[56]

A series of pyrimidine analogues in which a halogen atom is substituted at the carbon 5 position has been of particular interest in this context because of the specificity which some of these analogues exhibit with respect to incorporation into DNA versus RNA. When the analogue contains a fluorine atom, as in 5-fluorouracil (FU) or its deoxyriboside (FUDR), it may be incorporated extensively into RNA, but not at all into DNA;[28] instead, by blocking the enzymatic conversion of deoxyuridylic to thymidylic acid, the fluorinated analogues may interfere powerfully with DNA synthesis.[22] The converse is true of the other members of the series: 5-chloro-, 5-bromo-, and 5-iodouracil (ClU, BU, IU) and their corresponding deoxyribosides (ClUDR, BUDR, IUDR). The heavier halogen atoms of these analogues apparently resemble the methyl group of thymine sufficiently to enable their selective incorporation into DNA in the place of thymine. Several of the purine analogues have also been reported to undergo incorporation, usually of very limited extent, but their incorporation is less selective and involves both RNA and DNA.[9,39,42,60]

Interest in the radiobiologic implications of these phenomena was touched off by the observation of Greer[18] that thymine-deficient bacterial mutants grown on 5-BU were rendered manyfold more sensitive to ultraviolet radiation. It was soon reported that mammalian cells were also sensitized when grown in the presence of BUDR or IUDR and that sensitivity to ionizing radiation was likewise augmented in both bacterial and mammalian cells.[14,36] In the presence of competitive concentrations of thymine or thymidine, these analogues were much less effective or even inert, suggesting that their actual incorporation into DNA was a prerequisite for radiosensitization; moreover, the degree of sensitization was shown to depend on the extent of incorporation.[36] That the effect was specific for DNA-incorporated analogues was demonstrated by the failure of FU to alter radiosensitivity.[36] It was later found that the corresponding brominated analogue of deoxycytidine (BCDR), which undergoes metabolic conversion to BUDR inside the cell, is also active as a radiosensitizer in mammalian cells.[4] Sensitization has also been observed when BU is incorporated into bacteriophage[54] in which DNA is the sole nucleic acid.

Thus, analogues which are exclusively incorporated into DNA cause a striking change in the sensitivity of cells to the loss of reproductive integrity after irradiation. It follows logically that DNA must be in the major radiobiochemical pathway leading to this form of cell death. More direct evidence that the initial radiation insult actually occurs within the DNA molecule was provided by studies with bacterial transforming DNA, which can be irradiated either *in vivo* in the bacterial cell or *in vitro* after extraction and purification, after which it may be assayed for its loss of biologic activity. Transforming DNA into which BU had been incorporated was correspondingly more sensitive to ultraviolet irradiation than normal DNA, whether irradiated *in vivo* or *in vitro*.[44] Since the *in vitro* irradiations were carried out in the absence of RNA and protein, their participation in the radiosensitization phenomenon does not seem essential, and it may be concluded with some assurance that the primary radiobiochemical lesion leading to ultraviolet-induced cell death occurs in DNA. Unpublished preliminary observations indicate that the same conclusion also holds for roentgen rays.

Several of the purine analogues, notably thioguanine, 6-mercaptopurine, and 2-aminopurine, are also powerful radiosensitizers, despite the fact that the maximal extent of their incorporation is almost a hundredfold less than that of BU.[35,39] The purine analogue sensitizers are inactive when roentgen irradiation is carried out in an oxygen-free atmosphere, whereas the response to the pyrimidine analogues is unaffected,[38] suggesting that the molecular mechanisms involved are significantly different. These molecular mechanisms remain to be elucidated, although it has been demonstrated that BU is inherently more sensitive than thymine to degradation after ultraviolet or roentgen irradiation *in vitro* or in DNA *in vivo*.[5,52,53] It may be that the halogen atom augments the susceptibility of the pyrimidine ring to saturation of the C-5,6 double bond, with subsequent hydration and hydroperoxidation. Alternatively, it has been suggested by Szybalski[56] that the incorporation of BU into DNA may render the phosphate ester backbone of the molecule more vulnerable to breakage.

If DNA is indeed the macromolecule within which the radiobiochemical lesions leading to cell death occur, it might be expected that such parameters as DNA content, ploidy, and possibly base composition would correlate well with radiosensitivity in different classes of cells. Recently, advantage has been taken of the known differences in base composition which characterize different species of bacteria to investigate the influence of this parameter on radiosensitivity. It was found that the radiosensitivity of 8 different bacterial species increased linearly with the ratio of guanine and cytosine/adenine and thymine of their DNA.[37]

It has long been known that the nucleic acid "volumes" of viruses correlate well with their relative roentgen ray sensitivities. In recent years, reasonably accurate data have become available on the DNA content and radiosensitivity of several plant, animal, and bacterial viruses. Similar data for a few haploid and diploid microorganisms and for diploid cells of mammalian and avian species have also been reported. Terzi[58] has collated this material and found that the responses fall into four groups, differing by successive orders of magnitude in the lethality of radiation per ion pair. Another independent review of this literature, reported more fully elsewhere,[34] reveals a striking log-log correlation between nucleic acid content and radiosensitivity. The values for double-stranded DNA bacteriophages and haploid microorganisms appear to lie on one iso-sensitivity line, with a slope of 1.3. A parallel iso-sensitivity line, shifted tenfold in the direction of increased resistance, links the four available diploid cell values. Finally, data for a few RNA-containing animal and plant viruses lie on a third iso-sensitivity line, about tenfold more sensitive than the haploid DNA line. It is of interest that the data for two of the smallest known DNA-containing bacteriophages, ϕX174 and S13, also fall on this line; the DNA of these two phages has been shown to be single-stranded, resembling in this respect the RNA of the plant and animal viruses. Although data for many other viruses, bacteria, and diploid cells of other higher organisms will obviously be necessary to test this analysis more rigorously, the three iso-sensitivity lines suggest that radiosensitivity is indeed a function of DNA content, ploidy, and "strandedness."

However, as biologic complexity increases from the phages to the bacteria and yeasts, there is about a tenfold decrease in relative radiosensitivity. Similarly, at the diploid level, mammalian cells are several-fold more resistant than would be predicted by extrapolation from the microorganism data. Howard-Flanders[31] and Guild[20] have suggested that repair mechanisms, presumably enzymatic in nature, may play a much larger role than has hitherto been recognized and that only a small fraction of the lesions induced in DNA by radiation persist long enough to be expressed biologically. Such repair processes might well be more highly developed in the more complex cells of higher organisms and might therefore furnish a plausible explanation for their significantly decreased radiosensitivity. Systematic efforts to establish the existence and biochemical nature of such repair process in bacterial and mammalian cells may well open up an important new chapter in radiation biochemistry.

Stanford University School of Medicine
Stanford Medical Center
300 Pasteur Drive
Palo Alto, California

REFERENCES

1. Alexander. P., Hamilton, L. D., and Stacey, K. A. Disorganization of secondary structure in proteins exposed to ionizing radiations in solid state. *Nature*, London, 1959, *184*, 226–228.
2. Alexander, P., and Stacey, K. A. Cross-linking of deoxyribonucleic acid in sperm heads by ionizing radiations. *Nature*, London, 1959, *184*, 958–960.
3. Allen, J. M. The Molecular Control of Cellular Activity. McGraw-Hill Book Company, Inc., New York, 1962.
4. Bagshaw, M. A. Modification of radiosensitivity of hamster cells *in vitro*. *Nature*, London, 1962, *193*, 389–391.
5. Barszcz, D., and Shugar, D. Radiation chemistry of nucleic acids and their derivatives. I. Some pyrimidines, dihydropyrimidines, and hydrated pyrimidines. *Acta biochimica polonica*, 1961, *8*, 455–471.
6. Belman, S., Levino, E., and Troll, W. Effect of some chemical and physical agents on melting (Tm) of DNA. *Fed. Proc.*, 1962, *21*, 374.
7. Bernstein, M. H. Deoxyribonucleoproteins of cell nuclei; sensitivity to x-rays. *Nature*, London, 1954, *174*, 463.
8. Bessman, M. J., Lehman, I. R., Simms, E. S., and Kornberg, A. Enzymatic synthesis of deoxyribonucleic acid (DNA). *Fed. Proc.*, 1957, *16*, 153.
9. Bieber, S., Dietrich, L. S., Elion, G. B., Hitchings, G. H., and Martin, D. S. Incorporation of 6-mercaptopurine-S^{35} into nucleic acids of sensitive and nonsensitive transplantable mouse tumors. *Cancer Res.*, 1961, *21*, 228–231.
10. Bollum, F. J. DNA synthesis by enzymes from mammalian tissues; calf thymus polymerase. *Fed. Proc.*, 1959, *18*, 194.
11. Brenner, S., Jacob, F., and Meselson, M. Unstable intermediate carrying information from genes to ribosomes for protein synthesis. *Nature*, London, 1961, *190*, 576–581.
12. Butler, J. A. V. Changes induced in nucleic acids by ionizing radiations and chemicals. *Radiation Res.*, 1959, Suppl. 1, 403–416.
13. Creasey, W. A., and Stocken, L. A. Effect of ionizing radiation on nuclear phosphorylation in radio-sensitive tissues of rat. *Biochem. J.*, 1959, *72*, 519–523.
14. Djordjevic, B., and Szybalski, W. Genetics of human cell lines. III. Incorporation of 5-bromo- and 5-iododeoxyuridine into deoxyribonucleic acid of human cells and its effect on radiation sensitivity. *J. Exper. Med.*, 1960, *112*, 509–531.
15. Dunn, D. E., Smith, J. D., Zamenhof, S., and Griboff, G. Incorporation of halogenated pyrimidines into deoxyribonucleic acids of *Bacterium coli* and its bacteriophages. *Nature*, London, 1954, *174*, 305–307.
16. Ekert, B., and Monier, R. Structure of thymine hydroperoxide produced by x-irriadation. *Nature*, London, 1959, *184*, 58–59.
17. Fisher, W. D., Anderson, N. G., and Wilbur, K. M. Studies on nuclei. II. Effects of x-rays on deoxyribonucleoprotein from rat thymus. *Exper. Cell Res.*, 1959, *18*, 481–493.
18. Greer, S. Studies on ultraviolet irradiation of *Escherichia coli* containing 5-bromouracil in its DNA. *J. Gen. Microbiol.*, 1960, *22*, 618–634.
19. Gros, F., Hiatt, H., Gilbert, W., Kurland, C. G., Risenbrough, R. W., and Watson, J. D. Unstable ribonucleic acid revealed by pulse labelling of *Escherichia coli*. *Nature*, London, 1961, *190*, 581–585.
20. Guild, W. R. Radiation sensitivity of deoxyribonucleic acid. Paper delivered at Symposium on Implications of Organic Peroxides in Radiobiology, Argonne National Laboratory, 1962.
21. Hart, E. J., and Platzman, R. L. Radiation chemistry. In: Mechanisms in Radiobiology. Volume 1. M. Errera, and A. Forssberg, Editors. Academic Press, Inc., New York, 1961, pp. 93–257.
22. Hartmann, K. U., and Heidelberger, C. Studies on fluorinated pyrimidines. XIII. Inhibition of thymidylate synthetase. *J. Biol. Chem.*, 1961, *236*, 3006–3013.
23. Hems, G. Effect of ionizing radiation upon xanthosine in dilute aqueous solution. *Nature*, London, 1960, *185*, 525–526.
24. Hems, G. Effects of ionizing radiation on aqueous solutions of inosine and adenosine. *Radiation Res.*, 1960, *13*, 777–787.
25. Hevesy, G. Effect of roentgen rays on cellular division. *Rev. Mod. Physics*, 1945, *17*, 102–111.
26. Hokin, M. R., and Hokin, L. E. Protein synthesis and ribonucleic acid metabolism in mouse pancreas *in vitro* after whole body irradiation with x-rays. *J. Biol. Chem.*, 1956, *219*, 85–94.
27. Holmes, B. E., and Mee, L. K. Incorporation of

methionine S^{35} into proteins of Jensen rat sarcoma cells after irradiation of tumour. *Brit. J. Radiol.*, 1952, *25*, 273–278.

28. Horowitz, J., and Chargaff, E. Massive incorporation of 5-fluorouracil into bacterial ribonucleic acid. *Nature*, London, 1959, *184*, 1213–1215.
29. Howard, A. Influence of radiation on DNA metabolism. In: Ionizing Radiations and Cell Metabolism. G. E. W. Wolstenholme, and C. M. O'Connor, Editors. Little, Brown & Company, Boston, 1956, pp. 196–206.
30. Howard, A., and Pelc, S. R. Synthesis of desoxyribonucleic acid in normal and irradiated cells and its relation to chromosome breakage. *Heredity*, Suppl. 6, 1953, 261–273.
31. Howard-Flanders, P. Factors affecting radiation injury to DNA in bacteria and bacteriophage systems. In: Brookhaven Symposia in Biology No. 14. 1961, pp. 18–31.
32. Hurwitz, J., Bresler, A., and Diringer, R. Enzymic incorporation of ribonucleotides into polyribonucleotides and effect of DNA. *Biochem. & Biophys. Res. Comm.*, 1960, *3*, 15–19.
33. Jacob, F., and Monod, J. Genetic regulatory systems in synthesis of proteins. *J. Mol. Biol.*, 1961, *3*, 318–356.
34. Kaplan, H. S., and Moses, L. E. Manuscript in preparation.
35. Kaplan, H. S., Smith, K. C., and Tomlin, P. Radiosensitization of *E. coli* by purine and pyrimidine analogues incorporated in deoxyribonucleic acid. *Nature*, London, 1961, *190*, 794–796.
36. Kaplan, H. S., Smith, K. C., and Tomlin, P. A. Effect of halogenated pyrimidines on radiosensitivity of *E. coli. Radiation Res.*, 1962, *16*, 98–113.
37. Kaplan, H. S., and Zavarine, R. Correlation of bacterial radiosensitivity and DNA base composition. *Biochem. & Biophys. Res. Comm.*, 1962, *8*, 432–436.
38. Kaplan, H. S., Zavarine, R., and Earle, J. Interaction of oxygen effect and radiosensitization produced by base analogues incorporated into deoxyribonuclease acid. *Nature*, London, 1962, *194*, 662–664.
39. Lepage, G. A. Incorporation of 6-thioguanine into nucleic acids. *Cancer Res.*, 1960, *20*, 403–408.
40. Lett, J. T., Stacey, K. A., and Alexander, P. Crosslinking of dry deoxyribonucleic acids by electrons. *Radiation Res.*, 1961, *14*, 349–362.
41. Marmur, J., and Doty, P. Heterogeneity in deoxyribonucleic acids. I. Dependence on composition of configuration stability of deoxyribonucleic acids. *Nature*, London, 1959, *183*, 1427–1429.
42. Mattews, R. E., and Smith, J. D. Distribution of 8-azaguanine in nucleic acid of *Bacillus cereus. Nature*, London, 1956, *177*, 271–272.
43. Novelli, G. D., Kameyama, T., and Eisenstadt, J. M. Effect of ultraviolet light and x-rays on enzyme-forming system. *J. Cell & Comp. Physiol.*, 1961, *58*, 225–244.
44. Opara-Kubinska, Z., Lorkiewicz, Z., and Szybalski, W. Genetic transformation studies. II. Radiation sensitivity of halogen labeled DNA. *Biochem. & Biophys. Res. Comm.*, 1961, *4*, 288–291.
45. Ord, M. G., and Stocken, L. A. Biochemical lesion *in vivo* and *in vitro*. In: Mechanisms in Radiobiology. Volume I. M. Errera, and A. Forssberg, Editors. Academic Press, Inc., New York, 1961, pp. 259–331.
46. Osawa, S., Allfrey, V. G., and Mirsky, A. E. Mononucleotides of cell nucleus. *J. Gen. Physiol.*, 1957, *40*, 491–513.
47. Rosen, D., Brohult, S., and Alexander, P. Effects of gamma rays on solutions of human serum albumin. I. Sedimentation studies. *Arch. Biochem.*, 1957, *70*, 266–276.
48. Scholes, G., Ward, J. F., and Weiss, J. Mechanism of radiation-induced degradation of nucleic acids. *J. Mol. Biol.*, 1960, *2*, 379–391.
49. Scholes, G., and Weiss, J. Chemical action of x-rays on nucleic acids. *Exper. Cell. Res.*, 1952, Suppl. 2, 219–241.
50. Scholes, G., and Weiss, J. Chemical action of x-rays on nucleic acids and related substances in aqueous systems. II. Mechanism of action of x-rays on nucleic acids in aqueous systems. *Biochem. J.*, 1954, *56*, 65–72.
51. Scholes, G., and Weiss, J. Oxygen effects and formation of peroxides in aqueous solutions. *Radiation Res.*, 1959, Suppl. 1, 177–189.
52. Smith, K. C. Chemical basis for sensitization of bacteria to ultraviolet light by incorporated bromouracil. *Biochem. & Biophys. Res. Comm.*, 1962, *6*, 458–463.
53. Smith, K. C. Photochemistry of nucleic acids. In: Photophysiology. A. C. Giese, Editor. Academic Press, Inc., New York. To be published.
54. Stahl, F. W., Crasemann, J. M., Okun, L., Fox, E., and Laird, C. Radiation-sensitivity of bacteriophage containing 5-bromodeoxyuridine. *Virology*, 1961, *13*, 98–104.
55. Stevens, A. Incorporation of ribonucleotides into RNA. *Fed. Proc.*, 1961, *20*, 363.
56. Szybalski, W. Properties and applications of halogenated deoxyribonucleic acids. In: The Molecular Basis of Neoplasia. University of Texas Press, Austin, 1962, pp. 147–171.
57. Terasima, T., and Tolmach, L. J. Variations in several responses of HeLa cells to x-irradiation during division cycle. *Biophys. J.*, 1963, *3*, 11–33.
58. Terzi, M. Comparative analysis of inactivating

efficiency of radiation on different organisms. *Nature*, London, 1961, *191*, 461–463.

59. Van Bekkum, D. W. Oxidative phosphorylation in some radiosensitive tissues after irradiation. In: Ionizing Radiations and Cell Metabolism. G. E. W. Wolstenholme, and C. M. O'Connor, Editors. Little, Brown & Company, Boston, 1956, pp. 77–89.
60. Wacker, A., Kirschfeld, S., and Träger, L. Über den Einbau Purin-Analoger Verbindungen in die Bakterien-Nukleinsäure. *J. Mol. Biol.*, 1960, *2*, 241–242.
61. Wacker, A., Trebst, A., Jacherts, D., and Weygand, F. Über den Einbau von 5-bromouracil-2^{14}C in die Desoxyribonucleinsäure verschiedener Bakterien. *Z. Naturforsch.*, 1954, *9*B, 616–617.
62. Watson, J. D., and Crick, F. H. Molecular structure of nucleic acids; structure for deoxyribose nucleic acid. *Nature*, London, 1953, *171*, 737–738.
63. Weiss, S. B., and Nakamoto, T. On participation of DNA in RNA biosynthesis. *Proc. Nat. Acad. Sci.*, 1961, *47*, 694–697.
64. Whitmore, G. F., Till, J. E., Gwatkin, R. B. L. Siminovitch, L., and Graham, A. F. Increase of cellular constituents in x-irradiated mammalian cells. *Biochim. et biophys. acta*, 1958, *30*, 583–590.
65. Wohlhieter, J. A., Buzzell, A., and Lauffer, M. A. Effect of x-rays on nucleic acid isolated from tobacco mosaic virus. *Biochim. et biophys. acta*, 1960, *43*, 163–172.

QUANTITATIVE ASPECTS OF RADIATION LETHALITY AT THE CELLULAR LEVEL*

By J. E. TILL
TORONTO, ONTARIO, CANADA

I SHOULD like to begin with three quotations taken from the book by Paterson,[30] "The Treatment of Malignant Disease by Radium and X-Rays." The first is: "The value of radiation—indeed the whole basis of radiotherapy—rests on its capacity to destroy certain types of malignant growths *in situ* without at the same time producing destruction of the normal tissues in which the tumor is growing and which necessarily receive an equal dose of radiation." The second is: "It is one of the fundamental facts of radiotherapy that tumors vary in their sensitivity." The third is: "The term radiosensitivity is open to misconception and merits definition. As used here it is to be considered entirely synonymous with *local radiocurability* (*i.e.*, in the treated zone) and in no sense refers merely to *rate of regression* following radiation except in so far as the two, naturally, tend to run parallel."

These three quotations serve to stress three topics of great practical interest to the radiotherapist: First, the action of radiation on malignant growths compared with its action on normal tissue; second, the differences in sensitivity between different tumors; and third, the meaning of the term "radiosensitivity." It is the purpose of the author to discuss what contributions recent work in cellular radiobiology may be able to make toward an understanding of these topics.

COLONY-FORMING ABILITY AS A CRITERION OF RADIATION ACTION ON CELLS

The concept of radiosensitivity most commonly used by radiobiologists in considering the actions of radiation on malignant growths is the one introduced into mammalian cell radiobiology by Puck and Marcus[32] in 1956. This concept is that the important function of the cell in this regard, the function which should be used as the criterion of cellular radiosensitivity, is the ability of the cell to give rise by proliferation to a large number of descendants. This function is generally referred to by radiobiologists as the "proliferative capacity" or "reproductive integrity" of a cell. It is only cells possessing this function which would be expected to be able to repopulate a tissue or regenerate a tumor following irradiation. As pointed out by Puck and Marcus, the best experimental methods presently available for measuring this function are ones which test for the ability of an individual cell to multiply and form a colony of descendants. In their own work, this involved the use of tissue cultures, but methods are now available for studying the colony-forming ability of cells *in vivo*, as will be described below.

Since its introduction in 1956, the tissue culture technique for measuring colony-forming ability of mammalian cells has been used widely. A number of significant results have emerged. In their original work, Puck and his co-workers[32,33] demonstrated that the proliferative capacity of mammalian cells is very sensitive to radiation in comparison with the cells of lower organisms. These and subsequent studies have shown that, surprisingly, the radiosensitivity of proliferative capacity of mammalian cells is *not* strongly dependent on the tissue of origin of the cells, or even on the species of the cell donor, and that the proliferative capacity of normal cells is at least as sensitive, and perhaps more sensitive, than that of tumor cells. These studies have also demonstrated that other criteria of radiation action on cell proliferation may often be misleading. These include, for example, determinations of the mitotic index, or even measurement of total cell growth. This is because a certain limited amount of growth and proliferation can occur even in those cells in the irradiated population which have suffered a loss of colony-forming ability—these are the "abortive" colonies and the "giant" cells described by Puck and Marcus.[32]

---

* From the Physics Division, Ontario Cancer Institute, and the Department of Medical Biophysics, University of Toronto, Toronto, Ontario, Canada.

Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963. Part of the Symposium: The Fundamentals of Radiobiology; Chairman, Dr. Henry S. Kaplan, Palo Alto, California.

The tissue-culture techniques pioneered by Puck and Marcus have also been used to great advantage by a number of workers to elucidate the factors influencing mammalian cell radiosensitivity. The results of these studies have been used to construct simple models of the effects of radiation on cells *in vivo*, (see, for example, Elkind;[10] Lajtha and Oliver[24]). Though attractive, these models are hypothetical and require experimental verification. The *in vivo* techniques required for this verification are being developed, chiefly using the mouse as the object of experimentation, and the results of these *in vivo* studies may be expected to provide a wealth of new information of value to the radiotherapist.

Since the tissue-culture results are too extensive to discuss in meaningful fashion here, this presentation is limited to the *in vivo* findings, and examples of our own work on cells of normal mouse hematopoietic tissue *in vivo* shall be used.

IN VIVO TEST OF PROLIFERATIVE CAPACITY

Two principal techniques are available for *in vivo* investigation of the radiosensitivity of individual mammalian cells. The first to be developed was that of Hewitt and Wilson.[16] Their method is specifically suited to a study of the survival of proliferative capacity of tumor cells, using as the crite-

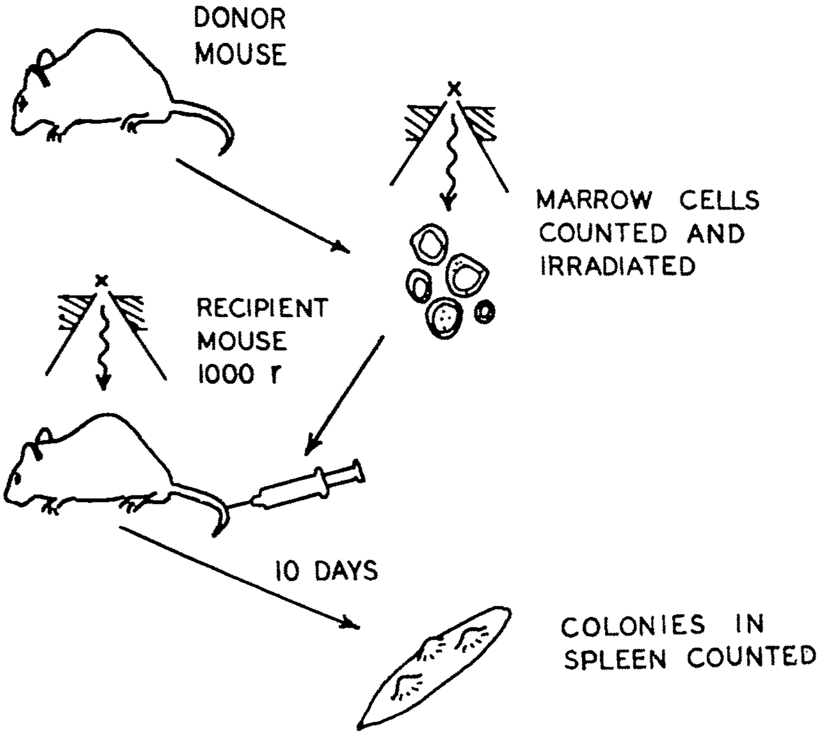

DONOR MOUSE
MARROW CELLS COUNTED AND IRRADIATED
RECIPIENT MOUSE 1000 r
10 DAYS
COLONIES IN SPLEEN COUNTED

Fig. 1. Diagrammatic illustration of the spleen-colony method[39] of testing for the proliferative capacity of marrow cells.

rion of proliferative capacity the ability of the irradiated cells to form tumors upon transplantation into new hosts. The minimum number of cells needed for successful transplantation is determined by an endpoint dilution procedure.

The second method to be developed was that of Till and McCulloch[39] which was specifically designed for the study of a normal cell population *in vivo*. The method is illustrated in Figure 1. It is based on a measurement of the ability of transplanted cells to colonize the spleens of supralethally irradiated mice. Here the criterion of proliferative capacity is the number of spleen colonies produced by the transplanted cells. Figure 2 shows the appearance of the colonies following fixation of the spleens in Bouin's solution. The spleen-colony method has recently been adapted to a study of the proliferative capacity of lymphoma cells by Bruce and Van der Gaag.[4]

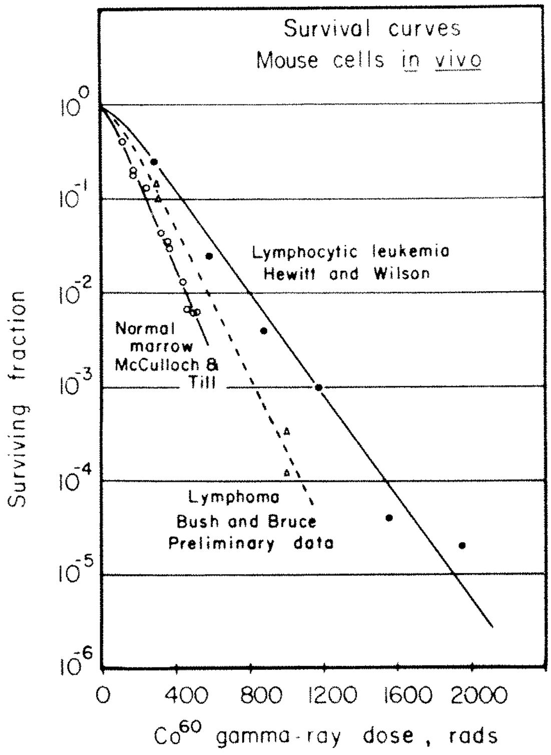


FIG. 3. Radiation survival curves for normal and malignant mouse cells proliferating *in vivo*.[5,16,26]

SURVIVAL CURVES

Examples of cell survival curves obtained by these methods are shown in Figure 3. These curves show an initial shoulder, then become straight lines on a semi-logarithmic plot. Such survival curves[1] may be characterized by a D_0 dose (the dose required to reduce the fractional survival by a factor of 0.37, on the exponential portion of the curve) and an extrapolation number (obtained by extrapolating the exponential portion of the curve back to zero dose and reading off the value of the ordinate). Survival curves of the type shown in Figure 3 may be used to predict the tumoricidal dose, *i.e.*, the dose required to destroy the proliferative capacity of all the cells in the tumor. For example, from the data of Hewitt and Wilson, a dose of approximately 2,000 rads reduces the surviving fraction to 10^{-5} of its original value. A dose twice as large, *i.e.*, 4,000 rads, should, therefore, reduce the surviving fraction to 10^{-10} of its original value. This would be sufficient to sterilize a tumor con-

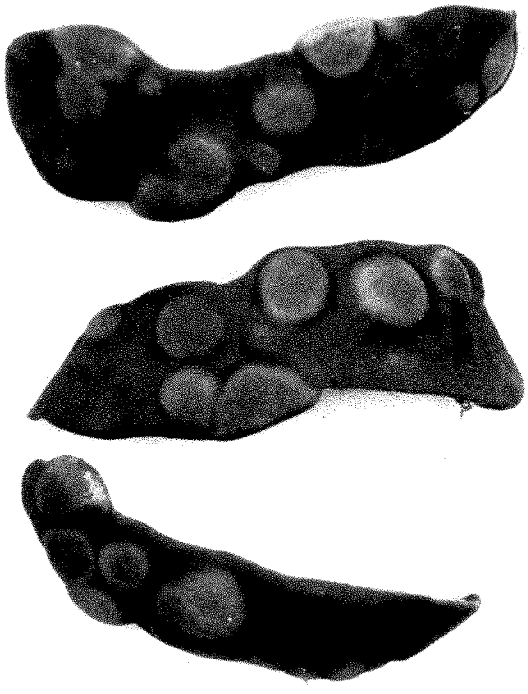


FIG. 2. Appearance of spleen-colonies following fixation in Bouin's solution.

taining of the order of a billion cells. Thus, it is apparent that predicted tumoricidal doses, based on experimental survival curves, are of the same order of magnitude as the doses actually used in radiotherapy.

The data shown in Figure 3 also indicate that, at best, individual tumor cells show the same radiosensitivity as normal marrow cells. At worst, they may be somewhat *less* sensitive. These very limited data thus support the same conclusion reached on the basis of the more extensive tissue-culture data mentioned earlier.

A summary of *in vivo* survival curve parameters taken from the literature is shown in Table I. The differences, though not large, are probably genuine.

MECHANISM OF INACTIVATION

Can one account for the possibility of differences in radiosensitivity between proliferating normal cells and tumor cells? The most favored hypothesis at present is that the principal mechanism of inactivation of mammalian cells by radiation is through the production of structural changes in chromosomes. Some evidence for and against this view is summarized in Table II.

This evidence will not be considered in detail, since it falls outside the main theme of this paper. However, if this view is correct, then the differences in radiosensitivity between cell lines, shown in Table I, are due primarily to differences in the chromosomal constitution of the different lines. Conclusive evidence that this is the case is lacking. It is, however, well known that the chromosomal constitution of tumor cells can be very variable, while that of normal cells is usually stable.[15]

The hypothesis that loss of proliferative capacity is due to damage to chromosomes could also explain the fact that the action of radiation on proliferating cells may be delayed, so that "abortive" clones of cells, capable of limited proliferation, may occur after irradiation. This delay could be due to a lag between the induction of genetic damage by radiation and phenotypic expression of this damage in the form of loss of some critical cell functions. Phenotypic lags of this sort are frequently observed in genetic studies on other systems.

MODIFICATION OF RADIOSENSITIVITY

The data shown in Figure 3 and Table I are somewhat disturbing. If tumor cells are often somewhat *less* sensitive than normal cells, what can be done to reduce the difference? A number of possibilities suggest themselves based on the extensive studies on cell cultures and on other organisms.

I. OXYGEN EFFECT

It is well known that oxygen acts as a radiosensitizing agent.[14] For example, the left half of Figure 4 shows the magnitude of the oxygen effect for normal mouse marrow cells.[41] The O_2 enhancement factor is 2.6. Is the enhancement factor more for tumor cells? A summary of some *in vivo*

TABLE I

SURVIVAL CURVE PARAMETERS FOR MOUSE CELLS IRRADIATED *in vivo* WITH COBALT 60 GAMMA RAYS UNDER OXYGENATED CONDITIONS

Cell Type	D_0,rads	Extrapolation No.	Reference
Normal marrow	95	1.5	McCulloch and Till[26]
Lymphocytic leukemia	$162 \times 0.97^{*} = 157$	Appr. 1.5	Hewitt and Wilson[16]
Lymphocytic leukemia (P-388)	160	1.6	Berry and Andrews[3]
Ascites carcinoma (Ehrlich)	$114/0.85^{**} = 134$	15.4	Hornsey and Silini[18]
Solid lymphosarcoma (6C3HED)	$110/0.85^{**} = 130$	1.2	Powers and Tolmach[31]

* Assuming 0.97 rads/r for Co^{60} radiation.[36]

** Assuming an RBE of 0.85 for Co^{60} gamma rays relative to 200–220 kvp. roentgen rays.[37]

TABLE II

SOME EVIDENCE BEARING ON THE HYPOTHESIS THAT FOR RADIATION-INDUCED LOSS OF COLONY-FORMING ABILITY OF MAMMALIAN CELLS THE PRINCIPAL TARGET FOR RADIATION DAMAGE LIES IN THE CHROMOSOMES

Evidence	Reference
In Support of the Hypothesis:	
1. Dose levels required to produce loss of colony-forming ability similar to those producing chromosome breaks	Puck[34]
2. Factors influencing the frequency of chromosome breakage also influence loss of colony-forming ability	Hornsey and Silini[19] Dewey and Humphrey[8]
3. Incorporation of 5-bromo-2′-deoxyuridine (BUdR) into the chromosomes increases the radiosensitivity of colony-forming ability	Djordjevic and Szybalski[9]
4. The stages of the division cycle most sensitive to radiation-induced loss of colony-forming ability are mitosis, and immediately prior to the initiation of DNA synthesis	Terasima and Tolmach[38]
5. The chromosomal constitution of the cells can influence their response to radiation	Whitfield and Rixon[44]
Not Supporting the Hypothesis:	
1. No strong dependence of the D_0 dose for loss of colony-forming ability on the ploidy or chromosome number content of the cells	Till[40]

data is shown in Table III. They suggest that the radiosensitivity of normal and tumor cells is dependent to a similar extent on oxygen concentration. Unhappily, however, there is evidence that tumor cell populations may often be at least partially anoxic, while normal cells are probably almost fully oxygenated.[8,17,31] Thus, instead of gaining from the oxygen effect, we may often lose.

Methods for taking into account the possibility of anoxia in tumor cell populations are being tested clinically. One may attempt to render both normal and malig-

TABLE III

COMPARISON OF THE D_0 DOSES FOR CELLS IRRADIATED *in vivo* WITH ROENTGEN RAYS OR WITH NEUTRONS IN THE PRESENCE OR ABSENCE OF OXYGEN

Cell type	D_0(roentgen rays)/ D_0(neutrons)		Oxygen enhancement ratio*		
	Oxygenated	Anoxic	Roentgen or gamma rays	Neutrons	Reference
Normal marrow	2.1	—	2.6	—	Till and McCulloch[41] Schneider and Whitmore[36]
Lymphocytic leukemia	—	4.3	2.3	—	Hewitt and Wilson[17] Andrews and Berry[2]
Ascites carcinoma (Ehrlich)	2.4	3.7	3.1	1.9	Hornsey and Silini[20]

* Oxygen enhancement ratio = D_0 (anoxic)/D_0 (oxygenated).

nant cells fully oxygenated,[14] or, conversely, one may attempt to make both normal and malignant cells anoxic. Another method now being considered utilizes the dependence of the oxygen effect on the type of radiation used.[11]

2. TYPE OF RADIATION

Several experimental studies (see, for example, Reference 7) have shown that the type of radiation used can greatly influence the loss of proliferative capacity produced by a given radiation dose. A comparison of the survival curves obtained for normal marrow cells irradiated with roentgen rays and with neutrons is shown in the right half of Figure 4 (data of Schneider and Whitmore[36]). It may be seen that the survival curve for neutrons shows both a reduced D_0 and a reduced extrapolation number. Collected *in vivo* data are included in Table III. Again, no difference between normal cells and malignant cells is apparent. However, it is of particular interest that Hornsey and Silini[20] found that the oxygen effect *in vivo* is less for neutrons than for roentgen rays. Other studies have supported this view and it has been suggested that neutron beams, properly used, might be advantageous in a situation where the tumor cells are anoxic while the surrounding normal cells are fully oxygenated.[11]

3. DOSE FRACTIONATION

The excellent *in vitro* work of Elkind[10] and co-workers has provided quantitative data concerning the extent to which dose fractionation can modify mammalian cell radiosensitivity. They demonstrated that recovery from radiation damage may occur during the time interval between dose fractions. Typical data, obtained for normal mouse marrow cells,[42] are shown in Figure 5. It may be noted that recovery reached an initial maximum after a 5 hour interval, then decreased to a minimum at 11 hours, then rose again.

One other study at the cellular level performed *in vivo* is that of Hornsey and Silini.[21] A comparison of the data is shown in Table IV. The initial maxima of recovery occurred at about the same time in

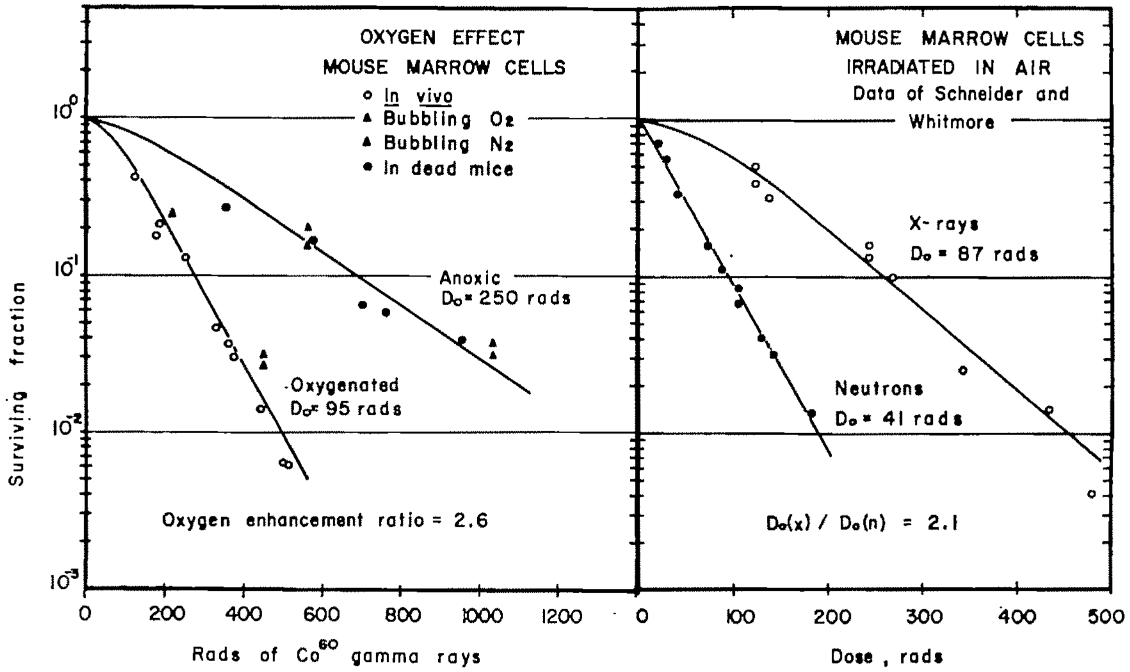


Fig. 4. *Left:* survival curves for normal marrow cells, illustrating the oxygen effect.[41] *Right:* survival curves for normal marrow cells irradiated with roentgen rays and neutrons.[36]

TABLE IV

RECOVERY BETWEEN FRACTIONATED DOSES *in vivo*, OXYGENATED CONDITIONS

Cell Type	Time of Initial Maximum of Recovery	Time of Intermediate Minimum	Reference
Normal marrow	5 hr.	11 hr.	Till and McCulloch[42]
Ascites carcinoma (Ehrlich)	6 hr.	?	Hornsey and Silini[21]

normal marrow cells and in Ehrlich ascites tumor cells. Unfortunately, the study of Hornsey and Silini was terminated shortly after the initial maximum was reached. It is not yet known whether or not an intermediate minimum can occur in their system, and if so, at what time. If the intermediate minima (or the maxima) were to occur at *different times* in normal cells compared to tumor cells, *selective killing of tumor cells by a suitable dose-fractionation regimen would be possible.* This possibility merits intensive study. Indirect evidence suggesting that such a possibility may be realized has been presented by Kallman.[22]

CELL PROLIFERATION KINETICS

Probably of greatest interest in considering the problem of dose-fractionation is the possibility that the kinetics of proliferation of the various normal and tumor cell types may be different. An example for normal mouse hematopoietic tissue is shown in Figure 6. The upper half of the Figure shows the kinetics of regeneration of colony-forming cells in the spleen following a dose of 400 rads.[43] The lower curve shows the kinetics of regeneration of colony-form-

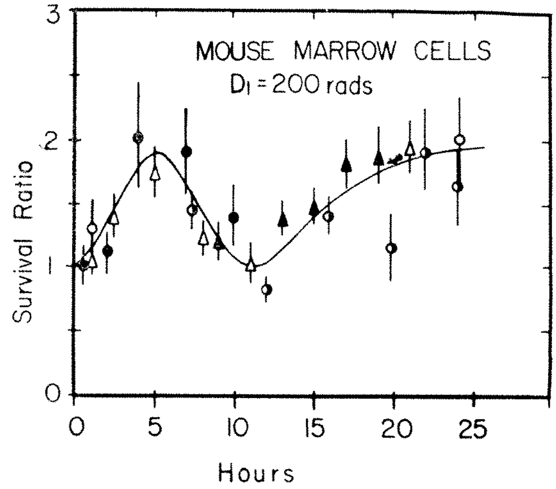


FIG. 5. Recovery of the proliferative capacity of marrow cells as a function of the time interval between two dose fractions of 200 rads each.[42] Ordinate: ratio of survival for the total dose delivered as two dose fractions to the survival for the same total dose given during a single exposure.

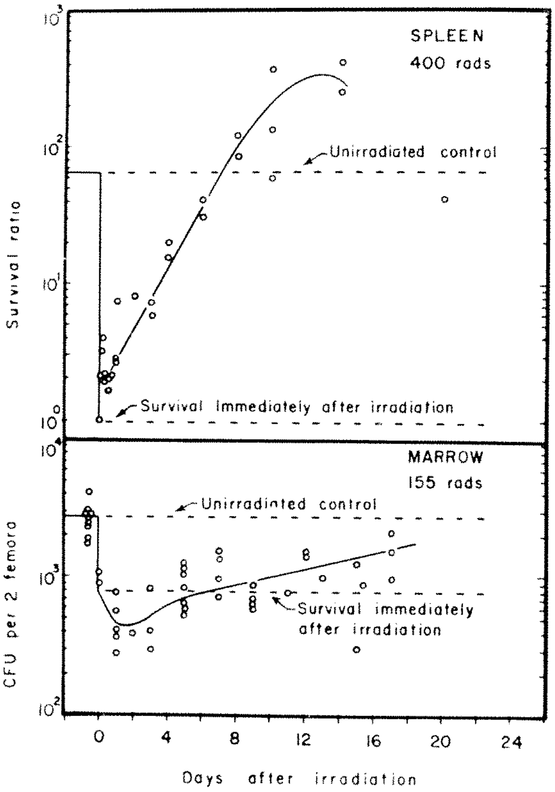


FIG. 6. Kinetics of proliferation of colony-forming cells in spleen and in marrow following irradiation. *Upper curve:* colony-forming cells in the spleen, following a dose of 400 rads.[43] Ordinate: survival of colony-forming ability relative to that observed immediately after irradiation. *Lower curve:* colony-forming units (CFU) per two femora, determined by the spleen-colony technique.

TABLE V

CONTENT OF COLONY-FORMING CELLS IN LYMPHOMAS OF AKR/J MICE FROM DATA OF BRUCE AND VAN DER GAAG[4]

Type of Tumor	No. of Determinations	Mean No. of Cells Required to Produce a Single Colony in the Spleen*
Spontaneous	15	1.1×10^4
Transplanted	8	1.9×10^2

* Not corrected for cells forming colonies in sites other than the spleen.

ing cells in femoral marrow following a dose of 155 rads.[27] It is apparent that the rates of regeneration are very different.

From the data shown in the lower half of the Figure for marrow, another phenomenon is evident. During the first day after irradiation, a detectable secondary loss of colony-forming cells occurred, presumably due to some process of cell removal. This phenomenon has also been detected by other means and its possible significance has been discussed.[25] No secondary loss of colony-forming cells in irradiated spleen is evident from the data shown in the upper half of Figure 6.

Comparison of the regeneration rates in spleen and marrow on the basis of the data of Figure 6 indicates that dose fractions of about 200 rads each, spaced a week apart, should depopulate the marrow colony-forming cell compartment without seriously affecting the colony-forming cell content of the spleen. It may be more than coincidence that this dose-fractionation regimen is very similar to that used to induce a high incidence of leukemia in mice.[23]

More studies of this type for various tumor cell populations as well as for different normal tissues are urgently needed. The few detailed studies that have been made of the kinetics of proliferation of tumor cell populations (see, for example, Mendelsohn[28]) indicate that tumor cells may be very heterogeneous with respect to growth parameters, so that a rational dose-fractionation scheme based upon a knowledge of these parameters might provide a way of selectively inactivating tumor cells in the presence of normal cells.

PROPORTION OF COLONY-FORMING CELLS

Another factor which might be expected to have an important influence on the response of a tumor or tissue to radiation is the proportion of colony-forming cells initially present. Recent work by Bruce and Van der Gaag[4] has indicated that the content of colony-forming cells in spontaneous lymphomas of strain AKR/J mice is much lower than in transplantable lymphomas obtained by serial passage of spontaneous tumors. Preliminary data are shown in Table v. These data suggest that the observation[6,30] that recurrences generally respond less well to therapy than the primary tumor might be, in part, due to differing contents of colony-forming cells.

RADIOSENSITIVITY OF TUMORS

One may attempt to summarize the factors which, on the basis of radiobiologic experimentation of the type described above, would be expected to contribute importantly to the response of a tumor to to irradiation. These factors are listed in Table vi. Some of these factors have already been considered by Lajtha and Oliver.[24]

Of particular importance from the practical point of view are those factors which affect the "therapeutic ratio,"[30] *i.e.*, the differential between the effects of radiation on tumor cells and the effects on normal cells. It has been stressed in this paper that proliferating normal cells are, if anything, *more* sensitive to radiation than are tumor cells. Taken at face value, this would imply that the therapeutic ratio should always be unfavorable. Radiotherapeutic experience proves that this is not so. How, then, does radiotherapy succeed? The main reason must be, of course, that the radiation is beamed toward the tumor and as little normal tissue as possible is irradiated. In addition, it is often possible to avoid the main vital normal tissues like marrow and intestinal epithelium, which require cell proliferation in order to function. It is probable that the function of nonproliferating normal tissues is, in general, not seriously affected by the dose levels used in radiotherapy. The main problem appears to be one of reducing to the lowest possible level the amount of damage to *proliferating* normal tissues which are unavoidably in the radiation beam, while at the same time giving a lethal dose to the tumor. There is still a great deal of radiobiologic work to be done on this problem, for example, toward the determination of optimal dose-fractionation procedures.

It should be stressed again that the clinical concept of radiosensitivity is often based on the behavior of the total cell population after irradiation, and a rapid rate of regression after irradiation is often assumed to be indicative of a high radiosensitivity. Many authors[6,30] have pointed out that such tumors may not be *radiocurable* in that they may frequently recur at some later time, either at the same site, or elsewhere. To the radiobiologist, the important index of radiosensitivity of tumors is the number of cells in the irradiated tumor which remain capable of continued proliferation, as tested, for example, by colony-forming ability. One might expect great improvement in the results of radiotherapy if a way could be found to test routinely for the number of colony-forming cells present in human tumors. It is very important that considerable effort be expended on attempts to do this. Indirect methods utilizing cytologic[12,13] and tissue-culture[29] methods have been reported with rather encouraging results. The development of a more direct technique would be of great value.

TABLE VI

SOME FACTORS AFFECTING THE RADIOCURABILITY* OF TUMORS

Factor	High Radiocurability	Low Radiocurability
1. Colony-forming cells outside the radiation field	no	yes
2. Dose-survival curves for colony-forming ability of tumor and normal cells	similar	different
3. Proportion of anoxic cells	low	high
4. Dose-fractionation schedule favors normal cells	yes	no
5. Tumor site favorable; few proliferating normal cells in the radiation field	yes	no
6. Rate of removal of cells after irradiation**	fast	slow
7. Rate of cell growth after irradiation	slow	fast
8. Proportion of colony-forming cells initially present	low	high
9. Number of surviving cells required to overcome host resistance and regenerate the tumor	high	low

* Radiocurable tumor: a tumor that is not regenerated following irradiation.

** This factor is probably most important in determining whether or not a tumor appears "radiosensitive," *i.e.*, rapidly decreases in size after irradiation.

SUMMARY

In summary, then, radiobiologic studies on normal and tumor cells of the mouse *in vivo* and extensive similar studies on normal and malignant cells proliferating in tissue culture, including human cells and cells derived from other mammals, have indicated that all proliferating mammalian cells have approximately the same intrinsic radiosensitivity as far as the effect of radiation on the proliferative capacity of the cells is concerned. In particular, tumor cells and proliferating normal cells do not differ greatly in sensitivity, with the tumor cells showing, if anything, the lesser radiosensitivity. Factors which modify the radiosensitivity of cells do not appear to act selectively on either tumor or normal cells. Of critical importance in assessing the action of radiation on a tumor cell population is a knowledge of how many cells in the irradiated tumor possess the capacity for unlimited proliferation and the kinetics of multiplication of these cells after irradiation. The greatest block to progress in the understanding of the differences in radiocurability between different human tumors is the lack of a direct method for determining the proliferative capacity of cells in human tumors. If such a method could be developed, a more rational approach to diagnosis and treatment would be possible.

The Ontario Cancer Institute
500 Sherbourne Street
Toronto 5, Ontario, Canada

REFERENCES

1. Alper, T., Fowler, J. F., Morgan, R. L., Vonberg, D. D., Ellis, F., and Oliver, R. Characterization of "type C" survival curve. *Brit. J. Radiol.*, 1962, *35*, 722–723.
2. Andrews, J. R., and Berry, R. J. Fast neutron irradiation and relationship of radiation dose and mammalian tumor cell reproductive capacity. *Radiation Res.*, 1962, *16*, 76–81.
3. Berry, R. J., and Andrews, J. R. Quantitative studies of radiation effects on cell reproductive capacity in mammalian transplantable tumor system *in vivo*. *Ann. New York Acad. Sc.*, 1961, *95*, 1001–1008.
4. Bruce, W. R., and Van der Gaag, H. Quantitative assay for number of murine lymphoma cells capable of proliferation *in vivo*. *Nature*, 1963, *199*, 79–80.
5. Bush, R. S., and Bruce, W. R. Personal communication.
6. Cade, Sir S. Malignant Disease and its Treatment by Radium. Second edition. Volume I. John Wright & Sons, Ltd., Bristol, England, 1948.
7. Deering, R. A., and Rice, R., Jr. Heavy ion irradiation of HeLa cells. *Radiation Res.*, 1962, *17*, 774–786.
8. Dewey, W. C., and Humphrey, R. M. Survival of mammalian cells irradiated at different phases of life cycle, as examined by autoradiography. *Nature*, 1963, *198*, 1063–1066.
9. Djordjevic, B., and Szybalski, W. Genetics of human cell lines. III. Incorporation of 5-bromo- and 5-iododeoxyuridine into the deoxyribonucleic acid of human cells and its effect on radiation sensitivity. *J. Exper. Med.*, 1960, *112*, 509–531.
10. Elkind, M. M. Radiation responses of mammalian cells. In: Fundamental Aspects of Radiosensitivity. Brookhaven Symposia in Biology, 1961, *14*, 220–245.
11. Fowler, J. F., Morgan, R. L., and Wood, C. A. P. Pre-therapeutic experiments with fast neutron beam from Medical Research Council cyclotron. I. Biological and physical advantages and problems of neutron therapy. *Brit. J. Radiol.*, 1963, *36*, 77–80.
12. Glücksmann, A. Panel discussion; radiation changes in carcinoma of cervix as revealed by cytology and their role in determining prognosis. *Acta Unio internat. contra cancrum*, 1958, *14*, 358–362.
13. Graham, R. M., and Graham, J. B. Cytologic prognosis in cancer of cervix; two year survival rates in randomized series. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *87*, 56–59.
14. Gray, L. H., Conger, A. D., Ebert, M., Hornsey, S., and Scott, O. C. A. Concentration of oxygen dissolved in tissues at time of irradiation as factor in radiotherapy. *Brit. J. Radiol.*, 1953, *26*, 638–648.
15. Hauschka, T. S. Chromosomes in ontogeny and oncogeny. *Cancer Res.*, 1961, *21*, 957–974.
16. Hewitt, H. B., and Wilson, C. W. Survival curve for mammalian leukaemia cells irradiated *in vivo*; (implications for treatment of mouse leukaemia by whole-body irradiation). *Brit. J. Cancer*, 1959, *13*, 69–75.
17. Hewitt, H. B., and Wilson, C. W. Survival curves for tumor cells irradiated *in vivo*. *Ann. New York Acad. Sc.*, 1961, *95*, 818–827.
18. Hornsey, S., and Silini, G. Studies on cell-survival of irradiated Ehrlich ascites tumour. II. Dose-effect curves for x-ray and neutron irradiations. *Internat. J. Rad. Biol.*, 1961, *4*, 135–141.
19. Hornsey, S., and Silini, G. Relationship between chromosome damage and cell viability in Ehrlich ascites tumors. Proceedings Second International Congress of Radiation Research, Harrogate, England, 1962.
20. Hornsey, S., and Silini, G. Pre-therapeutic experiments with fast neutron beam from Medical Research Council cyclotron. IV. Comparisons of effects of x-rays and cyclotron neutrons on mouse ascites tumours, mouse testis, and chick embryos. *Brit. J. Radiol.*, 1963, *36*, 92–97.
21. Hornsey, S., and Silini, G. Recovery of tumor cells cultured *in vivo* after x-ray and neutron irradiations. *Radiation Res.*, 1962, *16*, 712–722.
22. Kallman, R. F. Recovery from radiation injury; proposed mechanism. *Nature*, 1963, *197*, 557–560.
23. Kaplan, H. S., Brown, M. B., and Paull, J. Influence of bone-marrow injections on involution and neoplasia of mouse thymus after systemic irradiation. *J. Nat. Cancer Inst.*, 1953, *14*, 303–316.
24. Lajtha, L. G., and Oliver, R. Cell population kinetics following different regimes of irradiation. *Brit. J. Radiol.*, 1962, *35*, 131–140.

25. Lajtha, L. G., Oliver, R., and Gurney, C. W. Kinetic model of bone-marrow stem-cell population. *Brit. J. Haemat.*, 1962, *8*, 442–460.

26. McCulloch, E. A., and Till, J. E. Sensitivity of cells from normal mouse bone marrow to gamma radiation *in vitro* and *in vivo*. *Radiation Res.*, 1962, *16*, 822–832.

27. McCulloch, E. A., and Till, J. E. Measurement of proliferative capacity of mouse hematopoietic tissue, applied to irradiation of marrow *in vivo*. Proceedings of the American Association Cancer Research, 1961, *3*, 249.

28. Mendelsohn, M. L. Autoradiographic analysis of cell proliferation in spontaneous breast cancer of C3H mouse. III. Growth fraction. *J. Nat. Cancer Inst.*, 1962, *28*, 1015–1029.

29. Miller, N. F., Ludovici, P. P., Christian, R. T., and Riley, G. M. Irradiation sensitivity of cervix cancer; reponse of cultured cervix cells to irradiation. *Am. J. Obst. & Gynec.*, 1958, *76*, 1071–1082.

30. Paterson, R. The Treatment of Malignant Disease by Radium and X-Rays. Edward Arnold & Co., London, 1948.

31. Powers, W. E., and Tolmach, L. J. Multicomponent x-ray survival curve for mouse lymphosarcoma cells irradiated *in vivo*. *Nature*, 1963, *197*, 710–711.

32. Puck, T. T., and Marcus, P. I. Action of x-rays on mammalian cells. *J. Exper. Med.*, 1956, *103*, 653–666.

33. Puck, T. T., Morkovin, D., Marcus, P. I., and Ciecura, S. J. Action of x-rays on mammalian cells. II. Survival curves of cells from normal human tissues. *J. Exper. Med.*, 1957, *106*, 485–500.

34. Puck, T. T. Action of radiation on mammalian cells. III. Relationship between reproductive death and induction of chromosome anomalies by x-irradiation of euploid human cells *in vitro*. Proceedings National Academy of Sciences, 1958, *44*, 772–780.

35. Report of the International Commission on Radiological Units and Measurements (ICRU) 1959. National Bureau of Standards Handbook 78.

36. Schneider, D. O., and Whitmore, G. F. Comparative effects of neutrons and x-rays on mammalian cells. *Radiation Res.*, 1963, *18*, 286–306.

37. Sinclair, W. K. Relative biological effectiveness of 22-mevp. x-rays, cobalt-60 gamma rays, and 200-kvcp. x-rays. VII. Summary of studies for five criteria of effect. *Radiation Res.*, 1962, *16*, 394–398.

38. Terasima, T., and Tolmach, L. J. Variations in several responses of HeLa cells to x-irradiation during division cycle. *Biophys. J.*, 1963, *3*, 11–33.

39. Till, J. E., and McCulloch, E. A. Direct measurement of radiation sensitivity of normal mouse bone marrow cells. *Radiation Res.*, 1961, *14*, 213–222.

40. Till, J. E. Radiosensitivity and chromosome numbers in strain L mouse cells in tissue culture. *Radiation Res.*, 1961, *15*, 400–409.

41. Till, J. E., and McCulloch, E. A. Unpublished data.

42. Till, J. E., and McCulloch, E. A. Early repair processes in marrow cells irradiated and proliferating *in vivo*. *Radiation Res.*, 1963, *18*, 96–105.

43. Till, J. E., and McCulloch, E. A. Repair processes in irradiated mouse hematopoietic tissue. To be published.

44. Whitfield, J. F., and Rixon, R. H. Distinctive chromosome markers of normal and radioresistant derivatives of L strain mouse cells. *Exper. Cell. Res*, 1961, *23*, 412–415.

QUANTITATIVE ASPECTS OF RADIATION EFFECTS AT THE TISSUE AND TUMOR LEVEL*

By HARVEY M. PATT, PH.D.
ARGONNE, ILLINOIS

THE decay of a function or the death of an organism after irradiation may be more than a matter of the initial impact on its components. In the same sense, the cure of a tumor may be more than a matter of the apparent radiosensitivity of its individual cells. Whether we are concerned with unorganized (single cells), partially organized (tumors) or organized (tissues) cell populations, the production of new cells can be readily impaired by irradiation. Yet, the evolution and magnitude of cell depletion and restitution may differ considerably in the several instances. Because of the possibilities for interplay in an organized cell population, a tissue response can be greater or less than the combined response of its cell components in isolation.

During the past several years, important strides have been made in our understanding of cell population kinetics and of the radiosensitivity of individual cells in regard to their reproductive integrity. I should say at the outset that a complete analysis of the kinetics of cell depletion and restitution has not yet been accomplished in any *in vivo* system, normal or tumor, even after a single dose of ionizing radiation.[28] Nevertheless, it is now possible to make a more quantitative approach to interpretation of radiation effects at the tissue level and, as a consequence of such efforts, some generalizations may be formulated and some pertinent questions may be asked.

PROLIFERATIVE ACTIVITY

The activity that is most critical for survival after relatively small doses of radiation, and parenthetically of greatest interest to the radiation therapist, is the making of a new cell. The dose-response relationships for reproductive integrity, by which is meant the capacity for unlimited proliferation, are of the same general form for a variety of normal and tumor cells in culture. Hematopoietic, leukemic, and ascites tumor cells assayed *in vivo* show a similar response. The curves usually include an initial relatively refractory region or shoulder followed by a more or less exponential decline with higher doses. The shoulder seems to vary more than the final exponential slope, the reciprocal of the latter, or mean lethal dose, ranging from about 100 to 200 rads in most instances. The existence of a refractory period means that damage must be accumulated to produce the effect. Some of the implications of these findings have been considered recently by Elkind,[6,7] and by Lajtha and Oliver[15,16,24] among others.

An important factor in the development and repair of lesions is the rate of particular processes. Thus, the number of degenerating cells in an irradiated tissue will depend upon the rate at which cells enter and leave a degenerative phase. While degenerative changes, *e.g.*, early necrobiosis, can be independent of proliferative activity, the rate of proliferation is a factor in the rate of degeneration. The rate of proliferation of a cell depends on the cell cycle, *i.e.*, the time between successive mitoses. Now, it appears that the large differences in cell cycle times among various mammalian cells are due mainly to differences in the duration of the pre-DNA synthetic period.[28] Hence, the proportion of cells in other phases of the cell cycle, *e.g.*, DNA synthesis, mitosis, will

---

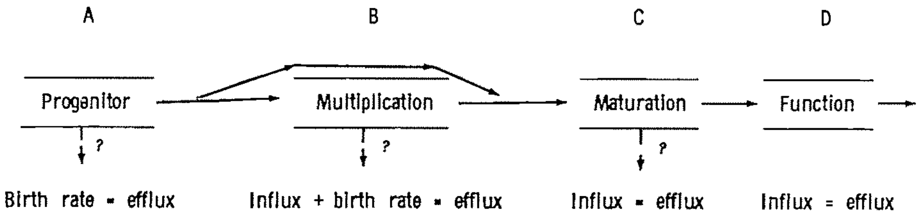
* Division of Biological and Medical Research, Argonne National Laboratory, Argonne, Illinois.

This work was performed under the auspices of the U. S. Atomic Energy Commission.

Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963. Part of the Symposium: The Fundamentals of Radiobiology; Chairman, Dr. Henry S. Kaplan, Palo Alto, California.

Table I

OPERATION CLASSIFICATION OF CELL RENEWAL SYSTEMS



Examples:

A-B-C-D	Bone marrow; seminiferous epithelium
A-C-D	Intestinal epithelium; epidermis

be increased when the cell cycle is short and decreased when it is long. If certain of these transitions are more radiosensitive than the pre-synthetic period, it is easy to see how an increased rate of proliferation might increase degenerative changes.

There is another consideration, however, owing to the fact that some forms of damage become manifest only when the cell attempts to divide, *i.e.*, in consequence of asymmetric mitoses. The duration of the initial mitotic block appears to be related to the length of the cell cycle and it turns out that mitoses return earlier in tissues considered to be more radiosensitive.[26] It seems that if an irradiated cell continues to divide, the second division will be less delayed than the first and the third one may be hardly delayed at all.[28] In other words, the change responsible for the initial mitotic delay tends to disappear with subsequent mitoses. This means that tissues consisting of rapidly proliferating cells may not only degenerate more rapidly, but may also recover more rapidly. If damage must be accumulated within a certain time to embarrass the reproductive integrity of a cell,[6] this time might be less for rapidly than for slowly dividing cells. The effect of dose protraction or fractionation would vary accordingly, which is to say that such procedures would have relatively less influence on the response of a slowly proliferating cell system.

CELL RENEWAL SYSTEMS AND STEM CELLS

The consequences of damage to radiosensitive cells will depend upon the dynamic organization of the system to which they belong. In many tissues of diverse origin, cell production and loss are delicately balanced so as to maintain a steady state with constant population.[18] Such cell renewal systems can generally be structured into compartments or classes of cells with specific attributes of form, function, or location. A theoretical analysis of the various transitions in a steady state cell population has been made recently by Quastler.[31] An operational (and minimal) classification of cell renewal systems is shown in Table 1. The progenitor compartment, as distinguished from the multiplicative compartment, is self-sustaining. This means that some cells retain their reproductive capacity indefinitely. The multiplicative compartment is merely an amplifier of production, consisting of differentiating cells that are destined to lose their fertility sooner or later. Thus, the crucial component for repopulation of a tissue is the progenitor compartment; a renewal sysem can recover from radiation damage only if some of the stem cells have preserved their function.

The identity of stem cells and their kinetics and regulation are very much a matter of conjecture. Presumably some cells in the intestinal crypts and basal layer of the epidermis function as stem cells; the

A type spermatogonia in the seminiferous epithelium and the primitive reticular cells in the bone marrow are thought to represent precursor cells. Several models have been suggested to account for the self-replenishment of stem cells. In one of these, there is thought to be a "bivalent" division in the sense that one daughter cell initiates differentiation while the other remains a stem cell. Since such a statistical concept is not particularly flexible and does not permit recovery of a depleted population, it has been proposed that stem cells can also undergo a "univalent" division, *i.e.*, produce two stem cells.[25] It is possible that cells capable of self-replenishment may undergo differentiation only after a sequence of divisions, with one or two of the progeny remaining as stem cells; this seems to be the situation in the testis. An alternative suggestion is that non-dividing stem cells can be induced to differentiate at random, *e.g.*, by a humoral factor, with the stem cell compartment maintained at a steady level by a mechanism regulating the number of dividing cells. This has been proposed for the bone marrow.[17]

In the intestinal crypts, there is apparently some sort of control of compartment size; the relative efflux of crypt cells is decreased during the initial period of recovery after irradiation and then increased as the crypts become repopulated.[28] If this were not the case, the stem cell compartment probably could not be reconstituted, since the cell generation cycle is already quite brief; it would either be depleted if a constant number of crypt cells continued to differentiate, or it would reach a new steady state at a lower level of stem cells if a proportionate number differentiated. The situation in the bone marrow is less clear. If only non-dividing stem cells can initiate differentiation, as postulated by Latjha *et al.*,[9,17] the random removal mechanism will be self-limiting; because of the control of compartment size, an increasing proportion of stem cells will proliferate and, hence, become unavailable for differentiation. Whatever the mechanism, an adjustment of stem cell outflow to the number of stem cells must also occur in the bone marrow.

The number of stem cells in a cell renewal system is germane to the kinetics of restitution. An excess of stem cells relative to normal requirements would facilitate recovery after a given irradiation, since even if the same fraction were rendered sterile, more intact stem cells would remain. An analogous situation probably contributes to changes in the cure rate of a given exposure for similarly constituted tumors as a function of size.[21] Comparatively few stem cells are required to restore a depleted population; only a few to a few dozen cells may suffice to repopulate the entire bone marrow because of the possibility of seeding.

GROWTH FRACTION

While the pattern of cell development will depend on the structure of a renewal system, the rate of development will be determined by other parameters as well. One of these is the proliferation rate or cell cycle time, which has already been discussed. Another is the growth fraction. The term "growth fraction" is not unequivocal; it is used most frequently to designate the fraction of cells that can divide in a population. In point of fact, all cells that can divide, or look as if they can, may not divide for various reasons.[28] This happens for example, in the intestinal crypts where only about half of the cells divide.

Tumors may have a variable growth fraction.[19] It is known that tumor cells as such divide no more rapidly than many types of normal cells. The doubling time of the most rapidly growing experimental tumors during the initial exponential phase of growth (approximately 10 to 15 hours) is about the same as the generation time of the proliferating elements in intestinal epithelium and bone marrow. During subsequent phases of tumor growth, the doubling time is usually considerably longer than the renewal time of many normal tissues (Table II).

Autoradiographic studies with tritiated

thymidine in several animal and human tumors reveal that comparatively few cells may be labeled.[1,11,12,19] While this could be due partly to the non-uniform distribution of thymidine in the tumors,[14] it is attributable also to the fact that many tumor cells are not in a mitotic cycle.

It is conceivable that all tumor cells, with the obvious exception of those that are degenerating in necrotic areas, may be fertile if not fecund. On the other hand, only a proportion of tumor cells may retain their reproductive integrity or, in other words, function as stem cells;[10] the remainder may lose fertility, perhaps because of a chromosomal imbalance although other phenomena may also be involved.[35] In either instance, that is, loss of fecundity or loss of fertility, tumor growth could be exponential for a time, if the "actual" growth fraction remained constant. If this fraction decreased as tumors enlarged, there would be a progressive decrease in rate of growth. Growth deceleration could also be associated with a progressive increase in the cell cycle time of the fecund cells and/or in the rate of cell loss from the tumor. This could account for the decelerating growth tendency even if the growth fraction were constant. The significance of such considerations in the evaluation of tumor growth has been discussed recently by Mendelsohn.[20] If only a fraction of cells in a tumor are actively proliferating, though others still retain their reproductive integrity, effective sensitization with, for example, halogenated pyrimidines might be difficult to achieve. Moreover, variability of the growth fraction could influence the effects of dose fractionation based on the tumor doubling time prior to irradiation.[15] Progressive depopulation will occur with a 50 per cent sterilizing dose if the interval between dose fractions is less than the doubling time. However, if the growth fraction should increase with continuing exposures (without change in cell cycle time), the doubling time will decrease, and in consequence so will the subsequent rate of depopulation unless the fractionation interval is also shortened.

Table II

RENEWAL RATE OF SEVERAL TISSUES IN THE MOUSE AND RAT*

Renewal System	Turnover Constant (cells/cell/day)	
	Tissue	Functional Cell
Myeloid Marrow	0.5	1.5 (granulocyte)
Erythroid Marrow	0.2	0.02 (erythrocyte)
Intestinal Epithelium	0.5	1.0 (villus)
Seminiferous Epithelium	0.05	0.1 (sperm)
Epidermis (Plantar)	0.02	0.025 (stratum corneum)

* Based on data in references 18, 22, 28, 30 and 41.

CELL TURNOVER AND FLOW PATTERNS

Factors other than the over-all cell birth rate can influence the flux patterns in a renewal system.[28] Death is not necessarily restricted to cells in the functional compartment. This is true for spermatogenesis as well as for hematopoiesis. In the latter, production rate may be "death-controlled," that is, adjusted by variations in the mortality of newly-formed cells. Moreover, the presumably orderly sequence of maturation compartments may be bypassed by shunts. Both the pattern of cell movements and the associated fluxes in a renewal system are critical in establishing relationships between the impaired cell production and the evolution of changes in the mature functional elements.

It is customary to refer to the turnover time of a cell renewal system or of its various compartments.[18] This has a definite meaning; namely, the time required to make, or to replace, a number of cells equal to the number in the system or compartment. Turnover time cannot necessarily be equated with generation or cell cycle time or with time required for the development of a particular cell. The latter, unlike the turnover time, will depend on many things including the number of successive divisions in the developmental sequence. For this reason alone, systems with identical turnover times may differ not only in kinetics of depletion, but also in the time for recovery. Turnover time is in many ways an ambiguous term. It represents the mean transit time, but if the population of a compartment is inhomogeneous, for example, consisting of cells with very slow and very rapid turnover, the mean transit time can be a meaningless parameter.[31] However, the reciprocal of the turnover time, which is the turnover constant, provides a useful index of relative fluxes. The turnover constant of a proliferating compartment is the birth rate plus influx, for a non-proliferating compartment the replacement rate, and for the entire system the renewal rate.

It will be noted in Table II that the turnover constant of seminiferous epithelium is about a tenth that of intestinal epithelium. Yet, temporary aspermia results from only a few hundred rads while a thousand or more rads are required for denudation of the villi.[23,32] The difference is related to the fine structure of the two systems and to the differential sensitivity and turnover of the various components. As regards the former, an important factor is the number of developmental steps required to make the functional cell; in other words, the time between stem cells in the crypts and villus cells is much shorter than that between stem cells in the testicular tubule and spermatozoa.[22,38] On the other hand, the turnover constants of erythroid and myeloid marrow cells are about the same. However, the rate of depression of the mature or functional cells (exclusive of loss due to extrinsic factors, *e.g.*, hemorrhage) and the rate of recovery are markedly different after similar irradiation. Erythrocyte and granulocyte developmental patterns are qualitatively similar and in this instance, the difference in depletion and recovery of functional cells is clearly related to differences in their turnover constants.

Quastler[33] has suggested that, as a rule, activities in progress are less susceptible to irradiation than the preparations for such activities. This means that a cell would be most susceptible at a period preceding the change from one activity pattern to another, for instance just prior to initiation of DNA synthesis or mitosis. The formulation of Bergonnié and Tribondeau,[2] which states that radiosensitivity of cells is proportional to the number of divisions and the degree of differentiation yet to be accomplished, can be derived from an association of sensitivity with change in activity pattern. Both cell division and differentiation involve sharp transitions. In general, when differentiation is well established, radiation may have little immediate influence on the kinetics of the subsequent maturation.[28] Blockage at various stages of the processes of maturation is less common than blockage of the various transitions in the proliferative cycle. This applies also to the decay of mature cells.

If cell production is blocked while transit through the maturation compartment remains unaffected, the population of mature (functional) cells should begin to decrease after an interval corresponding to the transit time. This is predicated on a fixed lifetime of maturing cells, *i.e.*, "first in, first out" kinetics. In several cell renewal systems, this relationship appears to hold after moderate irradiation; the onset of depression of mature cells is determined by the transit time of non-proliferating maturing cells (Fig. 1). A correspondence of this sort may not occur in all systems nor at all doses of radiation;[28] damage to maturing cells or to ancillary structures, for example, the vascular bed, and activation of homeostatic factors inhibiting or accelerating cell release could upset this simple kinetic relationship.

If there is no entry of cells into the functional compartment while cells exit at the usual time, the rate of depression of the functional cells will be determined by their turnover constants (Fig. 2). This may obtain for a brief period after irradiation, but in most cases the over-all situation becomes complex; as the system attempts to recover and the organism reacts to the injury, the kinetics of the system can deviate in a number of ways from normal. In the intestinal epithelium, which is one of the simplest renewal systems, there is a discrepancy of at least a factor of two between the time when complete denudation is expected (on the basis of "no production—normal exit") and the time when it actually occurs[38] (Fig. 3). This comes about because of partial efforts at proliferation, precocious maturation of some proliferative cells without intervening division, and alterations in the transitions of mature cells.[28]

Despite such departures from normal kinetics, knowledge of the normal situation can help to unravel species differences. The turnover of villus cells is faster in rat than in mouse, and depletion occurs more rapidly.[34] This could explain the greater sensitivity of the rat to intestinal death, assuming a similar blockage of cell production with a given radiation dose. In contrast, the turnover of blood granulocytes appears to be similar in a number of species. Yet, the time to reach a minimal level and to recover can vary considerably. This is apparently not related to the different times required for emptying of the maturation compartment nor to the initial rate of development of granulocytopenia, which is similar in the several species.[27] The kinetic patterns of the progenitor and multiplication compartments, and perhaps more importantly, the number of stem cells relative to production requirements may provide a basis for at least some of the differences in granulocyte depletion and recovery in the various species.

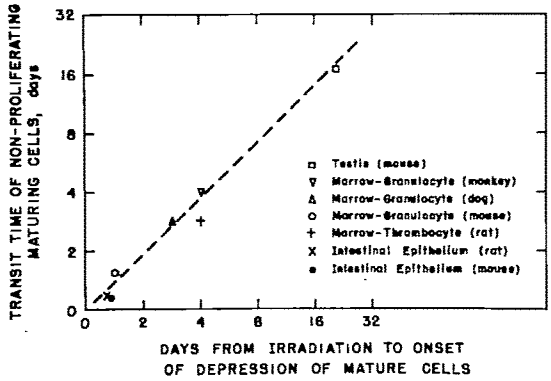


Fig. 1. Relationship of maturation time of nonproliferating cells to time of depression of mature cells. (Based on data in references 4, 8, 23, 27, 34 and 38).

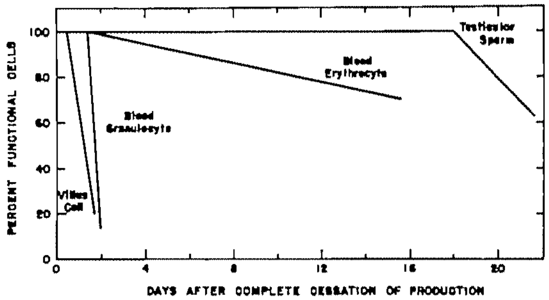


Fig. 2. Decay of mature cells in the x-irradiated mouse assuming complete blockage of production and no change in kinetics of maturing and mature cells.

When a minimum occupancy of the functional compartment is needed for survival, restitution must proceed simultaneously with depletion and must reach a sufficient level before depletion becomes critical. As noted earlier, the onset of a production deficit may precede the onset of a functional deficit (depopulation of mature cells)

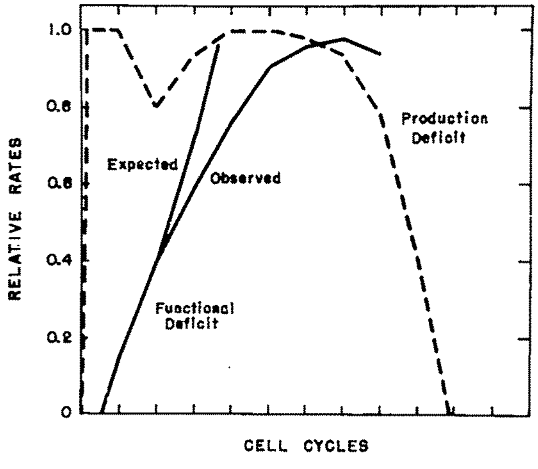


Fig. 3. The evolution of cell depletion in irradiated intestinal epithelium. (It is assumed that only 1 per cent of crypt cells retain reproductive integrity, the remainder dying during the first two cell cycles after the initial mitotic block. The expected and observed functional deficits are based on data reviewed in reference 28.)

by an interval approximately equal to the maturation time of the non-proliferating cells. The period of a proliferative deficiency and the period of a functional deficiency can overlap, depending on the turnover constants of the several compartments. This happens, for example, in the intestinal epithelium and in the granulocyte system, but the overlap occurs earlier in the former than in the latter. It turns out that regeneration is also more rapid in the intestine, perhaps in part because stem cell mobilization is not a requirement, and also because of the shorter developmental pathway, that is, essentially from stem cell to functional cell without an intervening multiplication compartment as in the case of hematopoietic tissue. In the testis, the delay between irradiation and onset of sterility is longer than the interval during which proliferation is suppressed unless large doses are used.[22] Thus, the functional deficit can occur after restitution has begun.

The comparative radiobiology of cell renewal systems has been treated recently in some detail by Patt and Quastler.[28] A few generalizations based on this analysis have already been stated. The "aplastic cytopenia" syndrome, characteristic of all cell renewal systems, has several distinct features. While the main problem in the depletion phase revolves about the impairment of cell production, other aspects of a cell renewal system may be affected. With total-body irradiation particularly, some of these may be a consequence of physiologic derangements outside of the system, for example, erythrocyte loss due to bleeding. Others may concern the system directly, for example, the extensive early killing of small lymphocytes. The central problem, however, is the interference with cell production, which can be brought about in at least three ways: early necrobiosis of proliferating cells, postirradiation freeze or blockage, and asymmetric mitosis.

We have seen that the kinetics of depletion are related to the normal kinetics of cell renewal but that the relationship may be only an approximate one. Flux patterns can become very complicated when a system is perturbed and, under such conditions, minor deviations, *e.g.*, altered decay of mature cells, maturation of sterile proliferative cells, may have great significance for survival of the system until recovery can be brought about. As emphasized earlier, this will occur only if a sufficient number of progenitor cells have retained their reproductive integrity.

Several factors enter into the kinetics of restitution. One is the possibility for mobilization of stem cells; this is believed to occur in the bone marrow.[17] An increase in net production without change in the growth fraction is possible where production is normally only partly efficient; this may also occur in the bone marrow. Acceleration of the generation cycle is probably not a factor in rapidly renewing tissues; in intestinal epithelia, active hair follicles, and bone marrow, the cell cycle is already very short. In intestinal epithelia, repopulation of the crypts is accomplished mainly by postponement of maturation. In comparatively slowly renewing systems such as the skin, shortening of the cell cycle may be more important in restitution. Under any circumstances, it is clear that return to the normal steady state condition can be achieved only by a favorable adjustment of the production rate to the withdrawal from the proliferative compartments.

As a rule, both depletion and restitution are more rapid in rapidly renewing systems. If the tempo of a system is depressed, for instance by low temperature in poikilotherms or by hibernation in mammals, depletion is depressed but so is restitution.[29] The question then is how can the return of successful proliferation be hastened without concomitant acceleration of a functional deficiency.

Some guidelines are suggested by the response of the liver to irradiation.[28] The parenchymal cells of the liver have a very low rate of proliferation and there is little obvious damage upon irradiation. When, however, the liver is forced to regenerate, latent damage is uncovered. Irradiation causes a delay in proliferative activity consequent to partial hepatectomy; this delay disappears slowly.[37] A second partial hepatectomy a week or so after the first decreases the lag in proliferative response. Hence, as noted previously, proliferative activity tends to reduce the inhibition. When proliferation is stimulated by partial hepatectomy after irradiation, much of the activity will be abortive due to chromosomal aberrations.[40] This, however, appears to be self-limiting; the number of chromosomal lesions revealed in this way declines with time and the rate of reduction approximates the division rate of the parenchymal cells. This decline can be accelerated by an increase in proliferation rate; since many of the damaged cells will be unable to proliferate successfully, the reproductive capacity of the regenerated liver will be greater than it was before.

In cell renewal systems in which there is a sufficient lag between the production deficit and a *critical* functional deficit, the processes of restitution might be compressed into a shorter period by a "forced regeneration." This might apply to systems such as epidermis, where the proliferation rate per cell might be increased, and to systems such as the bone marrow, where stem cells might be mobilized. There are indications that restitution can be accelerated somewhat in the hematopoietic system, *e.g.*, by procedures that result in early release of mature and maturing marrow granulocytes.[28]

Thus far, we have been concerned with total irradiation of cell renewal systems. Since this is rarely the case in therapy, a few remarks about partial irradiation are pertinent. Several kinds of cell interaction can occur when a system is only partially exposed. In a few instances, for example, the "reciprocal vicinity effect" in skin damage can be increased, presumably because of diffusion of a toxic material.[18] In most instances, however, damage is decreased by cell interaction. The most dramatic example is provided by hematopoietic tissue, mainly because of the transfer and seeding of progenitor cells, but reduction of damage occurs also in skin, cornea, and lens upon partial irradiation. This seems to be related to the increase in proliferative activity of the surrounding unirradiated tissue.[5] In any event, the possibility of cell interaction should be taken into account in the formulation of a radiation exposure pattern based on population kinetics of normal and tumor cells.

Unfortunately, there is considerably less information about the kinetics of tumor growth than about the kinetics of normal proliferating tissues. A tumor may begin as a homogeneous population, *i.e.*, a single cell, but as the population expands, the tumor can become quite heterogeneous with a variable growth fraction and cell generation cycle, a variable fraction of aneuploid and hypoxic cells, and a variable rate of cell loss. All of these factors are obviously pertinent to interpretation of the nature of tumor growth and its response to radiation and chemotherapeutic agents.

Whether a single irradiation is more efficient than a fractionated exposure depends on the desired effect. In general, one is inclined to say that a single exposure will be more efficient in those instances where recovery is possible. Where recovery constants of two systems differ sufficiently, dose-fractionation may lead to a considerable difference in the single dose equivalents.[15] The advantage of certain forms of dose-fractionation in tumor therapy has been known for a long time and the question may be asked whether the dose-time relationships that have been used are necessarily the most effective.[36] The answer must revolve around possible differences in kinetics of depletion and recovery of the tumor and of the unavoidably exposed normal tissues. However, another factor in a differential response to dose-fractionation is the possible contribution of "non-lethal effects" to the subsequent sensitivity of surviving cells over relatively long periods of time. Sensitivity may be decreased, *e.g.*, by polyploidy,[3] and increased, *e.g.*, by some physiologic change as shown in the small colonies derived from irradiated cells in culture.[39] Since a tumor is more than a bag of cells with some reproducitve integrity, we need to know much more about the various transitions that contribute to the cell flow patterns during the course of its expansion and reaction.

SUMMARY

The radiation response of a cell renewal system is more than a function of the intrinsic sensitivity of its components. The sequence of depopulation and repopulation depends upon the dynamic organization of the system. Although it is possible to relate the chronology of effects to normal kinetics, minor deviations of flow patterns and turnover constants can have profound significance for the fate of the system. As a rule, lesions develop faster and are repaired sooner in more rapidly renewing tissues. The rate of expansion of tumors may be much slower than the rate of renewal of many normal tissues. This probably accounts for at least some of the selective advantage of dose-fractionation. The various cell transitions and fluxes during tumor growth are not well understood, and further information about the kinetic patterns is germane to rationalization of therapeutic procedures.

Division of Biological and Medical Research
Argonne National Laboratory
9700 South Cass Avenue
Argonne, Illinois

REFERENCES

1. BASERGA, R., HENEGAR, G. C., KISIELESKI, W. E., and LISCO, H. Uptake of tritiated thymidine by human tumors *in vivo*. *Lab. Invest.*, 1962, *11*, 360–364.
2. BERGONNIÉ, J., and TRIBONDEAU, L. Interpretation of some results of radiotherapy and an attempt at determining a logical technique of treatment. (As translated by G. H. Fletcher from *Compt. Rend.*, 1906, *143*, 983–985.) *Radiation Res.*, 1959, *11*, 587–588.
3. BERRY, R. J. Quantitative studies of relationships between tumor cell ploidy and dose response to ionizing radiation *in vivo*. *Radiation Res.*, 1963, *18*, 236–245.
4. BRYANT, B. J., and KELLY, L. S. Autoradiographic studies of leukocyte formation. *Proc. Soc. Exper. Biol. & Med.*, 1958, *99*, 681–684.
5. DEVIK, F. Studies on cell population kinetics of x-irradiated and shielded mouse epidermis by autoradiography after administration of tritiated thymidine. *Acta path. et microbiol. scandinav.*, 1961, Suppl. 148, 35–41.
6. ELKIND, M. M. Cellular aspects of tumor therapy. *Radiology*, 1960, *74*, 529–541.
7. ELKIND, M. M. Radiation responses of mammalian cells. Fundamental Aspects of Radiosensitivity. *Brookhaven Symposia in Biology*, 1961, *14*, 220–245.
8. FEINENDEGEN, L. E., ODARTCHENKO, N., COTTIEF, H., and BOND, V. P. Kinetics of megacaryocyte proliferation. *Proc. Soc. Exper. Biol. & Med.*, 1962, *111*, 177–182.
9. GURNEY, C. W., LAJTHA, L. G., and OLIVER, R. Method for investigation of stem-cell kinetics. *Brit. J. Haemat.*, 1962, *8*, 461–466.
10. HAUSCHKA, T. S. Tissue genetics of neoplastic cell populations. *Canadian Cancer Conf.*, 1957, *2*, 305–345.
11. JOHNSON, H. A., HAYMAKER, W. E., RUBINI, J. R., FLIEDNER, T. M., BOND, V. P., CRONKITE, E. P., and HUGHES, W. L. Radioautographic study of human brain and glioblastoma multiforme after the *in vivo* uptake of tritiated thymidine. *Cancer*, 1960, *13*, 636–642.
12. JOHNSON, H. A., RUBINI, J. R., CRONKITE, E. P., and BOND, V. P. Labeling of human tumor cells *in vivo* by tritiated thymidine. *Lab. Invest.*, 1960, *9*, 460–465.
13. JOLLES, B., REMINGTON, M., and SIMON-REUSS, I. Indirect radiation effects and diffusible factors in irradiated tissues (Stromatex). *Acta radiol.*, 1961, *56*, 57–64.
14. KLIGERMAN, M. M., HEIDENREICH, W. F., and GREENE, S. Distribution of tritiated thymidine about a capillary sinusoid in a transplanted mouse tumour. *Nature*, 1962, *196*, 282–283.
15. LAJTHA, L. G., and OLIVER, R. Cell population kinetics following different regimes of irradiation. *Brit. J. Radiol.*, 1962, *35*, 131–140.
16. LAJTHA, L. G., and OLIVER, R. Some radiobiological considerations in radiotherapy. *Brit. J. Radiol.*, 1961, *34*, 252–257.
17. LAJTHA, L. G., OLIVER, R., and GURNEY, C. W. Kinetic model of bone-marrow stem-cell population. *Brit. J. Haemat.*, 1962, *8*, 442–460.
18. LEBLOND, C. P., and WALKER, B. E. Renewal of cell populations. *Physiol. Rev.*, 1956, *36*, 255–276.
19. MENDELSOHN, M. L. Autoradiographic analysis of cell proliferation in spontaneous breast

cancer of C3H mouse. III. Growth fraction. *J. Nat. Cancer Inst.*, 1962, *28*, 1015–1029.

20. Mendelsohn, M. L. Cell proliferation and tumour growth. In: Cell Proliferation. Edited by L. F. Lamerton, and R. M. J. Fry. Blackwell Scientific Publications, Oxford, England, 1963, 190–270.
21. Nice, C. M., Jr. Relation of tumor size to radioresistance. *Radiology*, 1957, *68*, 555–557.
22. Oakberg, E. F. Duration of spermatogenesis in mouse and timing of stages of cycle of seminiferous epithelium. *Am. J. Anat.*, 1956, *99*, 507–516.
23. Oakberg, E. F., and DiMinno, R. L. X-ray sensitivity of primary spermatocytes of mouse. *Int. J. Radiat. Biol.*, 1960, *2*, 196–209.
24. Oliver, R., and Lajtha, L. G. Problems of radiosensitivity in mixed cell populations with particular reference to radiotherapy. *Brit. J. Radiol.*, 1961, *34*, 659–666.
25. Osgood, E. E. Unifying concept of etiology of leukemias, lymphomas, and cancers. *J. Nat. Cancer Inst.*, 1957, *18*, 155–166.
26. Patt, H. M. Factors in radiosensitivity of mammalian cells. *Ann. New York Acad. Sc.*, 1955, *59*, 649–664.
27. Patt, H. M., and Maloney, M. A. Comparison of radiation-induced granulocytopenia in several mammalian species. *Radiation Res.*, 1963, *18*, 231–235.
28. Patt, H. M., and Quastler, H. Radiation effects on cell renewal and related systems. *Physiol. Rev.*, 1963, *43*, 357–396.
29. Patt, H. M., and Swift, M. N. Influence of temperature on response of frogs to x irradiation. *Am. J. Physiol.*, 1948, *155*, 388–393.
30. Price, D. Editor. Dynamics of Proliferating Tissues. University of Chicago Press, 1958.
31. Quastler, H. Cell population kinetics. *Ann. New York Acad. Sc.*, 1960, *90*, 580–591.
32. Quastler, H. Nature of intestinal radiation death. *Radiation Res.*, 1956, *4*, 303–320.
33. Quastler, H. Radiosensitive cell systems. In: Mammalian Aspects of Basic Mechanisms in Radiobiology. Edited by H. J. Curtis, and H. Quastler. NAS-NRC Publications 513, 1957, 19–57.
34. Quastler, H., Bensted, J. P. M., Lamerton, L. F., and Simpson, S. M. Adaptation to continuous irradiation: observations on rat intestine. *Brit. J. Radiol.*, 1959, *32*, 501–512.
35. Richards, B. M. Deoxyribose nucleic acid values in tumour cells with reference to stem-cell theory of tumour growth. *Nature*, 1955, *175*, 259–261.
36. Scanlon, P. W. Effect of mitotic suppression and recovery after irradiation on time-dose relationships and application of this effect to clinical radiation therapy. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *81*, 433–455.
37. Shapiro, I. M. Role of nuclear damage in regeneration of irradiated tissues. *Int. J. Radiat., Biol.*, 1961, *3*, 293–306.
38. Sherman, F. G., and Quastler, H. DNA synthesis in irradiated intestinal epithelium. *Exp. Cell Res.*, 1960, *19*, 343–360.
39. Sinclair, W. Personal communication.
40. Weinbren, K., Fitschen, W., and Cohen, M. Unmasking by regeneration of latent irradiation effects in rat liver. *Brit. J. Radiol.*, 1960, *33*, 419–425.
41. Widner, W. R., Storer, J. B., and Lushbaugh, C. C. Use of x-ray and nitrogen mustard to determine the mitotic and intermitotic times in normal and malignant rat tissues. *Cancer Res.*, 1951, *11*, 877–884.

INTRODUCTION TO SYMPOSIUM ON LYMPHOMAS*

By JAMES J. NICKSON, M.D.
NEW YORK, NEW YORK

HISTORICALLY, this symposium was born at a luncheon meeting called by our president, Dr. Fletcher, approximately 1½ years ago. It was the view of those attending the luncheon that the problem of optimal management of patients with early lymphoma was currently of considerable interest among those physicians concerned with the treatment of neoplastic disease. It seems evident that this interest has been stimulated by the observation, now in a number of clinics, that patients with localized lymphoma must be regarded as having cancer which is susceptible of long-range control. Indeed, the probability of such control appears to be distinctly higher than is the case for many epidermoid carcinomas that are regarded as being quite curable.

Accordingly, it seemed that a symposium which would consider the current status of our thinking on the management of this disease, and hopefully would stimulate us to think about how we might better manage such patients in the future, would prove profitable at the 1963 Annual Meeting.

The first paper, that on the clinical course of Stage I malignant lymphoma by Dr. Scheer, arises out of the rather curious fact that in the literature no article has been found dealing with the issue of the sites of involvement of patients with Stage I lymphoma who do develop recurrences. In Stage I cases of lymphomas, the thought that the contiguous or adjacent areas should be treated and that, if such treatment is given, the prognosis of the patient is improved assumes that there is contiguous spread from the area of known contamination. If this assumption is correct, there should then be some correlation between the sites in which disease is found next and the site of initial occurrence. In Dr. Scheer's paper an analysis is made of patients of the class noted above, who have received treatment and were followed subsequent to treatment at Memorial Hospital.

Dr. Lukes' paper is based upon his opportunities to study Hodgkin's disease while Chief of the Hematopathology Section of the Armed Forces Institute of Pathology, where the availability of 3,000 cases of Hodgkin's disease represents an enormous source of information. His ideas with regard to correlation between histology and prognosis are most stimulating.

Dr. Vera Peters who discusses the results of treatment of lymphomas has been instrumental in directing our attention to the fact that patients with early disease do well if aggressively treated.

Chemotherapy has found increasing use in the past decade in the treatment of all stages of lymphomas. It is felt that in knowledgeable hands, these agents are of distinct benefit in the management of selected patients. However, there is a strong suspicion in the minds of many of us that its use in the treatment of most patients with localized or regional lymphomas is not wise, and that the use of these agents is contraindicated if they are employed as a substitute for radiation therapy. Dr. Karnofsky, who has been associated with the chemotherapy of lymphomas since his war time days with the Chemotherapy Warfare Service, presents his views on the use of chemical agents in the treatment of early lymphomas.

It is our hope that this symposium will provide the stimulus for more studies devoted to better treatment for these patients. We are convinced that such patients should be treated with the intent of long-range control of their disease. Any lesser objective is unworthy.

Department of Radiation Therapy
Memorial Hospital for Cancer and
Allied Diseases
New York 21, New York

---

* Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963.

VOL. 90, NO. 5

THE COURSE OF STAGE I MALIGNANT LYMPHOMAS FOLLOWING LOCAL TREATMENT*

By ALAN C. SCHEER, M.D.
NEW YORK, NEW YORK

THIS study was undertaken in an attempt to document the "spread" of early malignant lymphoma from its primary source. The purpose of tracing the spread of Stage 1 disease is to provide a basis for the decision to treat prophylactically areas other than the ones known to be involved.

Certain assumptions are implicit in the prophylactic treatment of these diseases. One is that the patient's life will be prolonged if these tumors are suppressed before they become clinically manifest. The effectiveness of this treatment in terms of survival can be demonstrated only by randomized prospective study. Another assumption is that the diseases are sufficiently predictable in their courses so that the treatment will be delivered to areas most likely to be secondarily involved. It is this latter point which is to be discussed.

For the purpose of this presentation the words "primary," "recurrence," and "spread" are used in ways not commonly associated with malignant lymphoma. "Primary" refers to the lymph node area or organ in which the disease is first discovered. "Recurrence" refers to the second appearance of the disease in other than the primary area. "Spread" implies that the disease has reached the area of recurrence from the primary site. Most physicians who have dealt with these diseases have definite ideas about the multicentricity of lymphomas; but with the recently stimulated interest in prophylactic treatment, it seems reasonable to approach the problem without prejudice.

The over-all impression gained from the current literature seems to be that there has been improvement in the early prognosis of patients with these diseases. This may be because of more vigorous local and supportive treatment or because of prophylactic treatment, or perhaps because of other factors such as early diagnosis. Whatever the reason, there is much more optimism expressed by physicians who are treating these diseases today than was common a generation ago.

MATERIAL

The material studied includes all patients registered at Memorial Hospital from 1935 to 1957 with a definite diagnosis of one of the malignant lymphomas. There were 1,200 cases filed under the diagnosis of Hodgkin's disease and 1,500 cases were classified as lymphosarcoma or reticulum cell sarcoma.

The patients presented here have met the following criteria:

1. *No treatment prior to being seen at Memorial Center.* This permits only biopsy at the referring institution, even if the biopsy removed the only clinically involved lymph node. It does not permit the inclusion of patients who underwent adequate excisional surgery, such as gastrectomy or radical neck dissection.

2. *Pathology confirmed in our laboratory.* Only those patients are included who have had acceptable specimens submitted. Smears from aspiration biopsy are not considered acceptable, nor are specimens which are reported as "malignant lymphoma, favor Hodgkin's disease," for example.

3. *No other areas of involvement detected,* clinically or roentgenographically. This determination is made on the basis of

---

* Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963. Part of the Symposium: Lymphomas; Chairman, Dr. James J. Nickson, New York, New York.

Table I

HODGKIN'S DISEASE

STAGE I

Site	No. of Patients	No. of 5 Yr. Survivors
Neck	55	38 (69%)
Axilla	9	7
Groin	3	1
Mediastinum	1	1
	—	———
	68	47 (69%)

physical examination, chest roentgenogram and blood cell count. Abdominal roentgenograms, such as intravenous pyelograms or lymphangiograms, were not done routinely during the period studied, nor were bone marrow aspirations part of routine evaluation.

4. *No systemic manifestation.* This excludes patients with recent weight loss, fever, generalized itching, or anemia.

5. *Treatment given only to clinically involved area*, surgery and/or radiation therapy. Two important groups are excluded by this criterion. The larger is the pediatric group. It has been the custom in the Department of Pediatrics to supplement local radiation therapy with a systemic agent. The other large excluded group is reticulum cell sarcoma of bone. During the period of this study, it was the custom of the Bone Service, Department of Surgery, to give systemic therapy for these tumors, in addition to local surgery or radiation therapy. In addition, many of the patients who presented themselves with mediastinal lymphomas also received systemic therapy.

6. *Followed at least 5 years by members of staff of Memorial Center or died within that time.* This last criterion is the one which has excluded more patients than any other. Only those patients who kept follow-up appointments and were examined by members of our staff have been included. If a patient failed to keep his appointments and returned at some later date with evidence of disease in more than one anatomic area, he was excluded. In addition, patients were excluded if their follow-up was by mail even if a physician from some other institution attested to their survival and freedom from disease.

This may seem excessively rigid and certainly has reduced the number available for the study, but I think it gives assurance that the patients included are more likely to supply the information desired. (Parenthetically, it should be added that the exclusions have probably improved the survival percentages.) It is a tribute to the follow-up system that so few patients presented themselves at the appointed examination with recurrent disease in more than one area.

RESULTS

Hodgkin's disease. Table 1 shows the location of the primary tumor of the 68 patients with Hodgkin's disease included. As most writers report, the neck is the commonest site of involvement. The number of patients surviving 5 years is also included and is consistent with reports of survival in Stage 1 Hodgkin's disease from other centers. Figure 1 is a graphic representation of

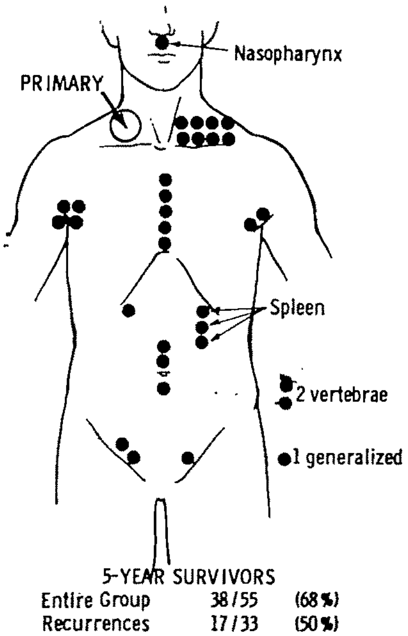


Fig 1. Sites of next involvement in 55 patients presenting with Hodgkin's disease in neck only.

Table II

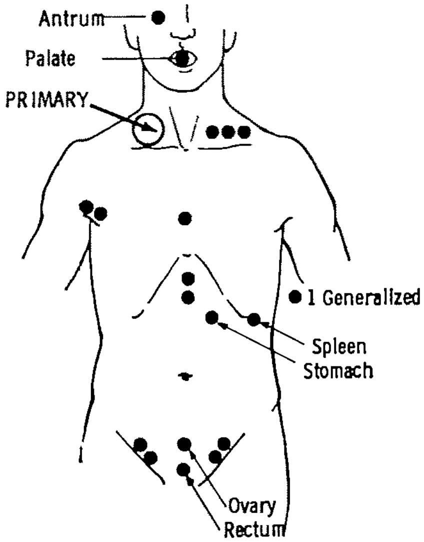
HODGKIN'S DISEASE

INCIDENCE OF PROXIMAL RECURRENCES

Primary Site	No. of Patients	No. of Proximal Recurrences
Neck	55	17
Axilla	9	3
Groin	3	1
Mediastinum	1	0
	—	—
	68	21*

* 10 survived 5 years.

the 55 patients who presented themselves with disease in the neck only. All tumors have been arbitrarily assigned to the right side of the neck for purposes of illustration. The actual ratio of right to left is 30:25. The dots on the figure indicate the site of next appearance of disease, and it will be seen that only one of these carefully followed patients appeared with generalized disease. The 5 year survival figures suggest that even those patients with recurrent disease have a reasonable chance of prolonged survival.



5-YEAR SURVIVORS
Entire Group 23/31 (74%)
Recurrences 11/19 (58%)

Fig. 2. Sites of next involvement in 31 patients presenting with lymphosarcoma in neck only.

Table II shows the number of patients in whom the second manifestation of their disease was in the "proximal areas." "Proximal recurrences" are defined as those which occur in the contiguous lymph node bearing areas; and for the neck, include the opposite side of the neck, the mediastinum, and the axilla on the same side. As can be seen, approximately one-third of the patients in all groups of primary involvement have the second appearance of the disease in these areas. These are the areas for which some authors have advocated prophylactic treatment.

Table III

LYMPHOSARCOMA

STAGE I

Site	No. of Patients	No. of 5 Yr. Survivors
Neck	31	23 (74%)
Tonsil	10	8
Stomach	8	7
Axilla	6	3
Groin	5	5
Orbit	3	2
Nasopharynx	2	2
Mediastinum	2	2
Naris	2	0
Epitrochlear	2	2
Miscellaneous*	6	4
	—	—
	77	58 (75%)

* Spleen, appendix, mesentery, cecum, breast, antrum.

Lymphosarcoma. Table III shows the sites of primary involvement in 77 patients with lymphosarcoma. Here one can observe a wider distribution of primary sites than is the case for Hodgkin's disease. The percentage of 5 year survivals suggests that primary tumors in the neck carry the same prognosis as the over-all group. Figure 2 shows graphically the sites of secondary involvement; and again, there is only 1 patient with generalized disease which was observed at an appointed follow-up visit. In this smaller group there are only 6 "proximal recurrences" out of 31 patients.

Reticulum cell sarcoma. Table IV lists the

TABLE IV

RETICULUM CELL SARCOMA

STAGE I

Site	No. of Patients	No. of 5 Yr. Survivors
Neck	20	11 (55%)
Axilla	7	4
Stomach	5	3
Tonsil	4	4
Groin	3	2
Mediastinum	2	0
Thyroid	2	1
Antrum	2	1
Miscellaneous*	8	6
	53	32 (60%)

* Cheek, chest wall, palate, nasopharnyx, naris, tongue, bladder, spleen.

areas of primary involvement in reticulum cell sarcoma. As might be expected, there is again a diversity of anatomic sites. The 5 year survival figures suggest that primary disease in the neck is fairly typical of the entire group as far as immediate prognosis is concerned. Figure 3 is a graphic representation of the patients with primary disease in the neck and shows proximal recurrences of the same order of frequency as seen in lymphosarcoma.

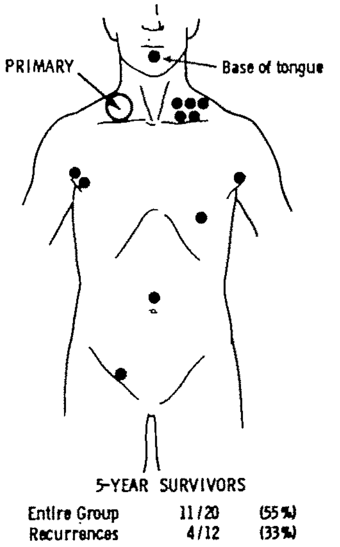


FIG. 3. Sites of next involvement in 20 patients presenting with reticulum cell sarcoma in neck only.

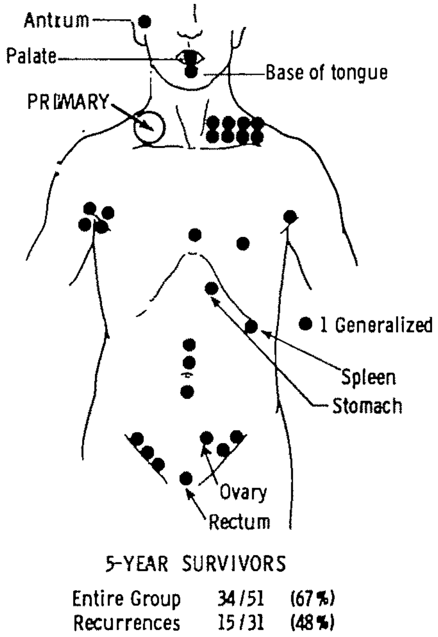


FIG. 4. Sites of next involvement in 51 patients presenting with lymphosarcoma and reticulum cell sarcoma in neck only.

Comparative evaluation. Figure 4 shows the combined picture for lymphosarcoma and reticulum cell sarcoma. It is not suggested that these terms can be used interchangeably; but many physicians feel that reticulum cell sarcoma and lymphosarcoma are variations of the same disease, reticulum cell sarcoma occurring in a somewhat older age group over-all, but both tumors being found at almost any age.

Finally, in Figure 5 the lymphosarcoma-reticulum cell sarcoma group is contrasted with the Hodgkin's disease group. These two groups contain about the same number of patients and seem to have about the same 5 year prognosis. The distribution of secondary involvement is quite similar.

CONCLUSIONS

Since Hodgkin's disease is uncommon in the pediatric age group, and since pediatric lymphosarcoma is excluded from this study because of the chemotherapy given to these

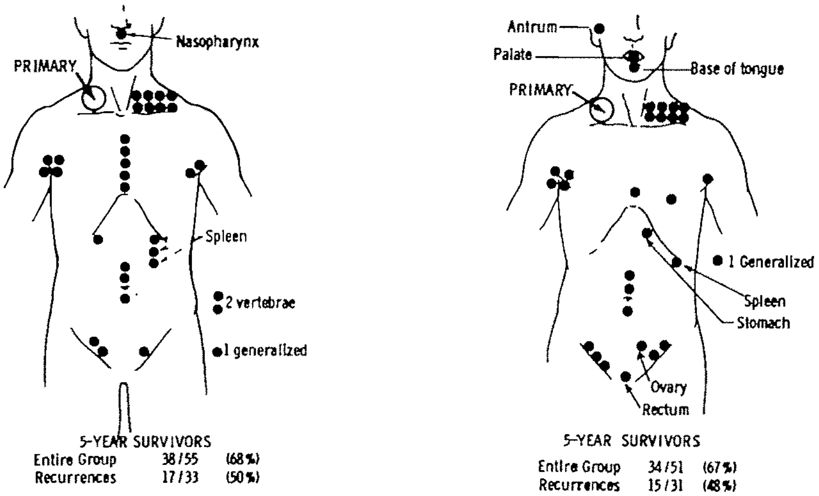


Fig. 5. *Left:* Sites of next involvement in 55 patients presenting with Hodgkin's disease in neck only (see Fig. 1). *Right:* Sites of next involvement in 51 patients presenting with lymphosarcoma and reticulum cell sarcoma in neck only (see Fig. 4).

children at Memorial Hospital, the conclusions must be confined to postpediatric Stage I malignant lymphoma cases.

The first conclusion is that the secondary manifestations of malignant lymphoma ("recurrences") seem to be fairly randomly distributed over the body, and very little, if any, difference exists among the specific diseases in this regard. However, among those patients whose "recurrences" have been identified during the follow-up period, there seems to be some preponderance of "recurrences" in the "proximal areas," particularly in Hodgkin's disease.

The short term prognosis, as measured by 5 year survival in carefully followed patients, seems to be similar for Hodgkin's disease and the lymphosarcoma-reticulum cell sarcoma group. The chance of developing generalized lymphoma; that is, disease in more than one area as the second manifestation, is relatively small. Therefore, staging of lymphomas other than Hodgkin's disease has some prognostic significance.

Even in patients who show "spread" beyond the treated area during follow-up period, long survivals are possible. The site of recurrence; that is, "proximal recurrences" as opposed to more distant "spread," is not of prognostic significance. Of the patients with Hodgkin's disease who had "proximal recurrences," there were 10 5 year survivors, the same proportion as the over-all 5 year survival rate in the patients with "recurrences." However, constant vigilance and prompt treatment of "recurrences" is required to produce these long survivals.

Adequate treatment consists of a high dose local radiation therapy to include the entire area of involvement with as wide a margin of normal tissue as possible. There is no indication at present for extending this treatment into adjacent uninvolved areas, beyond the point necessary to ensure an adequate margin.

If prophylactic treatment is thought desirable, the principle would seem to apply equally to the lymphosarcoma group and to Hodgkin's disease. However, the seemingly random distribution of secondary involvement provides little basis for the selection of fruitful areas to treat.

Department of Radiation Therapy
Memorial Sloan-Kettering Cancer Center
444 East 68th Street
New York 21, New York

RELATIONSHIP OF HISTOLOGIC FEATURES TO CLINICAL STAGES IN HODGKIN'S DISEASE*

By ROBERT J. LUKES, M.D.
LOS ANGELES, CALIFORNIA

THE significance of the wide variation in histologic features in Hodgkin's disease has perplexed pathologists since the initial microscopic studies of Greenfield in 1878 and provided the basis for the still existent controversy over the precise nature of the disease. Clinicians have been similarly puzzled by the different clinical forms varying from a fulminating febrile form of a few months' duration to a prolonged asymptomatic course of 15 or more years.

A direct relationship between survival and lymphocytic proliferation associated with infrequency of abnormal reticulum cells was reported first by Rosenthal.[16] The description of the paragranuloma type of Hodgkin's disease by Jackson and Parker,[6] however, represented the initial association of histologic features with localized disease manifestations and slowly progressive disease. This association has been supported by Harrison[4] in a study of prolonged survivors and also by Wright.[21] The distinctive histologic character of this lymphocytic proliferation, however, was sufficient for Smetana and Cohen[18] and Bonenfant[1] to question its relationship to Hodgkin's disease and stimulate Robb-Smith[15] to propose the term "lymphoreticular medullary reticulosis" and Lumb[10] "reticular lymphoma" for this lesion. The sarcomatous type of Jackson and Parker[6] relates a predominant proliferation of neoplastic reticulum cells of the Reed-Sternberg type with rapidly progressive disease. Similar observations were recorded by Smetana and Cohen,[18] but the rarity of the sarcoma type as an initial manifestation and the resemblance to reticulum cell sarcoma limited its significance. Neither Winterhalter[20] nor Croizat *et al.*[2] however, were able to find definite evidence of a relationship between the histologic features and the course of Hodgkin's disease. The widely used classification into paragranuloma, granuloma, and sarcoma proposed by Jackson and Parker[6] appears to have gained only limited support. The infrequency of paragranuloma and sarcoma has resulted in the inclusion of the great majority of all cases in granuloma and limited the prognostic value of the classification.

The application of a clinical staging method by Peters[12] to survival studies in Hodgkin's disease and in the evaluation of the effectiveness of radiation therapy without regard to histologic classification presented a new analytic approach. The extent of involvement when therapy was instituted was regarded by this author as the most important factor in survival. Localized lymphadenopathy, Stage I, was observed with prolonged survival and effective therapy while generalized involvement, Stage III, was associated with rapidly progressive disease and poor response to therapy. Intensive radiation therapy of the involved lymph nodes and the proximal region was believed to improve the survival rates. Similar observations on the value of clinical staging in survival have been reported by Jelliffe and Thomson[7] and also by Lumb and Newton.[11] The recent study of Peters and Middlemiss[13] provided further support for the significance of clinical staging and also evidence of the importance of systemic symptoms in staging as a valuable refinement in this approach. A study on the relationship of the histologic changes in involved lymph nodes to the existent clinical stages, however, has never been presented.

---

* From the Armed Forces Institute of Pathology and the Veterans Administration Central Laboratory for Anatomic Pathology and Research, AFIP, Washington, D.C.

Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963. Part of the Symposium: Lymphomas; Chairman, Dr. James J. Nickson, New York, New York.

The results of a morphologic study by Lukes, Butler, and Hicks[9] on 377 U.S. Army cases of Hodgkin's disease diagnosed during World War II (1942–1945) on the evaluation of the significance of the histologic features and clinical stages in survival will be presented in detail elsewhere. The purpose of this presentation will be to record the observations on the relationship between the histologic features and clinical stages from this study.

METHOD AND MATERIAL

The coded U.S. Army cases of Hodgkin's disease in the files of the Armed Forces Institute of Pathology on which a pretherapy lymph node biopsy was performed between January 1, 1942 and December 31, 1945 were reviewed independently by 2 pathologists (Robert J. Lukes and James Butler). Cases were considered acceptable only if diagnostic Reed-Sternberg cells were found. These cases were then classified according to: (1) the predominant histologic feature into the following histologic types—(a) lymphocytic and histiocytic nodular, (b) lymphocytic and histiocytic diffuse, (c) nodular sclerosis, (d) mixed, (e) diffuse fibrosis, (f) reticular; and (2) the types of Jackson and Parker[6]—(a) paragranuloma, (b) granuloma, (c) sarcoma.

Clinical staging was performed independently by a third person (Ethel B. Hicks) by the method of Peters[12] and entirely on the basis of the recorded observations in the clinical charts. Follow-up information was obtained on all 377 cases through either the Army or the Veterans Administration. Completed questionnaires were returned by all the surviving cases in the 15–18 year follow-up period.

Survival studies were performed on the following groups: (1) clinical stages of Peters according to both the initial method[12] and occurrence of systemic symptoms,[13] (2) histologic types based on predominant histologic features, (3) histologic types of Jackson and Parker,[6] (4) combined clinical stages and histologic types based on predominant histologic features, and (5) combined clinical stages and histologic types of Jackson and Parker.[6] The survival data were analyzed by accepted statistical methods by members of the Section of Medical Statistics of the Armed Forces Institute of Pathology.

The case population of this study is very similar to that used by Smetana and Cohen,[18] but the purpose and approach of the study differ greatly.

CASE POPULATION

This study of 377 U.S. Army cases from 1942–1945 is essentially an analysis of Hodgkin's disease in young American males of military age. The group is composed of 370 males (98 per cent) and 7 females (2 per cent). There are 360 Caucasians (95 per cent) and 17 Negroes (5 per cent). The observed ratio of Caucasians to Negroes of 2:1 is based on the 10 per cent Negro incidence in the Army during this period and is similar to that observed by others.[3,5] The age distribution reflects that of the Army population. There are 282 cases (75 per cent) between the ages of 18 and 30 and only 12 (3 per cent) in the 5th and 6th decades. The distribution of cases according to intervals is the following: 18–20 years—22 cases (6 per cent), 3rd decade—260 cases (69 per cent), 4th decade—83 cases (22 per cent), and 12 cases (3 per cent) in the 5th and 6th decades. The median age is 25 years. There is no significant difference in the median age of the patients in the various histologic groups.

CLINICAL STAGES

The distribution of the cases into clinical stages according to the method of Peters[12] is recorded in Table I along with the median survival and the number of survivors. On the basis of clinical staging alone it is apparent that there is a definite relationship between clinical stage and survival. The cases appear to be rather uniformly distributed according to stages with 38 per cent in Stage I, 34 per cent in Stage II, and 28 per

TABLE I

DISTRIBUTION AND SURVIVAL BY CLINICAL STAGE

Clinical Stage	Total No. of Cases	Total Per Cent	Survival (median year)	No. of Survivors*
I	142	38	9.1	51
II	127	34	3.2	5
III	108	28	1.3	0
All Stages	377	100	4.0	56

* Number of patients surviving 15 years.

cent in Stage III. The frequency of Stage III, however, seems unusually high for an Army population where personnel must be capable of full duty or be observed by a physician. Conversely, that the majority of these cases (72 per cent) are in Stages I and II is understandable under these conditions. The prolonged median survival of 9.1 years in the Stage I group assumes considerable importance in this case population when the largest portion was initially observed in this stage. It suggests that the opporunity for observing early disease manifestations existed, and a large proportion of patients with Stage I disease may remain quiescent for many years. The contrasting median survivals in Stage II and III, 3.2 and 1.3 years respectively, suggest that there are two forms of Hodgkin's disease, quiescent manifested clinically by Stage I and progressive manifested by Stage II and III. That 51 of 56 cases, or 91 per cent are in the 15 year survival period in the Stage I group supports this contention.

The interval between the reported onset of symptoms and/or signs and the intial histologic diagnosis of Hodgkin's disease did not vary significantly with the stages. The median interval was 4.5 months for the entire group, 4.5 months for cases in Stage I, 3.9 months in Stage II, and 5 months in Stage III. The clinical abnormalities recorded in this interval were related primarily to the patient's observation of an enlarged lymph node, particularly in Stages I and II. The true onset of symptoms and /or signs was often vague and inaccurate. The difficulty in dating the onset of clinical symptoms and signs accounts for the reliance on the biopsy date as the basis for the survival studies. The brief duration of the interval between apparent onset and the biopsy date and the limited variation between the stages suggest that this period is not a significant variable in this study.

The distribution of the 5, 10, and 15 year survivors according to clinical stages is recorded in Table II. In Stage I the incidence of survivors at each period is in striking contrast to the other two stages. It is apparent, however, that a number of patients presenting with manifestations of Stage II and III do survive 5 years and a few 10 years. Only 4 per cent of those in Stage II and none in Stage III reached 15 years. The incidence of survival for the entire group at each period is 40 per cent at 5 years, 22 per cent at 10 years, and 15 per

TABLE II

5, 10, AND 15 YEAR SURVIVAL ACCORDING TO CLINICAL STAGE (377 CASES)

Clinical Stage	Total No. of Cases	Survival 5 Year No.	Survival 5 Year Per Cent	Survival 10 Year No.	Survival 10 Year Per Cent	Survival 15 Year No.	Survival 15 Year Per Cent
I	142	100	70	67	47	51	36
II	127	38	30	13	10	5	4
III	108	13	13	2	2	0	0
Total	377	151	40	82	22	56	15

Table III

INFLUENCE OF SYSTEMIC SYMPTOMS ON 5, 10, AND 15 YEAR SURVIVAL IN RELATIONSHIP TO CLINICAL STAGES*

Clinical Stage	Total No. of Cases	5 Year		10 Year		15 Year	
		No.	Per Cent	No.	Per Cent	No.	Per Cent
No symptoms	219	135	62	81	37	56	26
I	142	100	70	67	47	51	36
IIA	55	26	47	12	22	5	9
IIIA*	22	9	41	2	9	0	0
With symptoms	158	16	10	1	0.6	0	0
IIB	72	12	17	1	1.4	0	0
IIIB	86	4	5	0	0	0	0
Total	377	151	40	82	22	56	15

* The clinical stages of Peters have been slightly modified by the recognition of an asymptomatic Stage III, designated Stage IIIA.

cent at 15 years. There is a remarkable similarity of this group which is almost exclusively male (98 per cent) to the male component in the study by Peters and Middlemiss.[13] In this latter group there was an identical survival of 40 per cent at 5 years and very similar incidence of 24 per cent at 10 years. The incidence at 15 years for each sex was not reported in their study. Further valid comparison of survival in individual stages or on the influence of systemic symptoms in staging is impossible due to the almost exclusive male population in this study and the aggregate method of recording data on both sexes in the studies of Peters and Middlemiss,[13] Jelliffe and Thomson,[7] and Lumb and Newton.[11]

The influence of systemic symptoms on 5, 10, and 15 year survival rates is recorded in Table III. A special group, Stage IIIA, was set aside for evaluation since a significant number of patients with the distribution of involvement of Stage III were observed without systemic symptoms. In general, the presence of systemic symptoms is a poor prognostic sign regardless of the distribution of involvement indicated by clinical stages. Systemic symptoms are a significant factor in the subclassification of Stage II, but recognition of Stage IIIA is also of importance since the 41 per cent incidence of 5 year survivals in this group is 8 times as high as in those with systemic symptoms.

HISTOLOGIC FEATURES

The description of the histologic types and the evaluation of their significance in survival will be presented in detail elsewhere.[9] The following histologic types were established on the basis of the author's experience with over 3,000 cases of Hodgkin's disease while Chief of the Hematopathology Section of the Armed Forces Institute of Pathology from 1954–1962: (a) lymphocytic and/or histiocytic,* nodular, (b) lymphocytic and/or histiocytic, diffuse, (c) nodular sclerosis, (d) mixed, (e) diffuse fibrosis, and (f) reticular. The variation in the histologic components within these types is schematically portrayed in Table IV. Although there is an extraordinary variation in the histologic findings in the lymph nodes of Hodgkin's disease, the following general features appear to exist. (1) There is an inverse relationship between the frequency of lymphocytes and abnormal reticulum cells of the Reed-Sternberg cell type. (2) Two distinctive types of connective tissue proliferation may be found—(a) a disorderly distributed, finely fibrillar

---

* The groups designed lymphocytic and/or histiocytic will be referred to as "L & H" hereafter with the modification of the nodular or diffuse type.

Table IV

SCHEMATIC REPRESENTATION OF VARIATION IN MORPHOLOGIC FEATURES IN HISTOLOGIC TYPES OF HODGKIN'S DISEASE

Histologic Groups	Lymphocytes	Histiocytes	Eosinophils	Plasma Cells	Fibrillar Reticulum	Collagen	Reed-Sternberg Cells
Lymphocytic and/or Histiocytic							
Nodular	++++++++	+	o	o	o	o	+
Diffuse	++++++	+++	o	o	o	o	+
Nodular sclerosis	+ to ++++	o to ++	+	+	+	+ to ++++	+
Mixed	+	++	+	+	++	o	++
Diffuse fibrosis	o	+	+	+	+++++	o	++
Reticular	+	o	++	+	o	o	+++++

type which in severe degree is designated diffuse fibrosis and (b) true collagen formation which occurs in interconnecting bands that isolate nodules of lymphoid tissue and is characteristic of nodular sclerosis. (3) Diffuse fibrosis is associated with lymphocytic depletion. (4) A variety of reticulum cells is found in Hodgkin's disease. These include: (a) the abnormal reticulum cells of the Reed-Sternberg cells with large nucleoli in all histologic types, (b) the peculiar polypoid reticulum cells found primarily in L & H types and nodular sclerosis, and (c) reactive reticulum cells or histiocytes which have abundant pale eosinophilic cytoplasm and large vesicular nuclei without prominent nucleoli.

Separation of the cases into the various histologic types is usually accomplished with ease. It is admittedly difficult in a small proportion of the cases and somewhat arbitrary since the mixed type exhibits a spectrum of histologic components and occupies an intermediate position between diffuse fibrosis and the reticular type at one extreme and diffuse type of L & H at the other. Designation of a lesion as either diffuse fibrosis or reticular type is dependent upon the predominance of either fibrillar connective tissue or Reed-Sternberg cells and a marked decrease in lymphocytes. At the opposite extreme the mixed type may also be somewhat difficult to separate from the L & H diffuse type when lymphocytes are numerous. In this situation the mixed type is selected when there is a prominent increase in eosinophils or the formation of fibrillar reticulum or both. L & H nodular type and nodular sclerosis appear to be fairly distinctive from the remaining types, but at times bear a resemblance to each other when the collagen band formation of nodular sclerosis is limited and lymphocytic proliferation predominates.

SURVIVAL ACCORDING TO HISTOLOGIC TYPES

The distribution of the cases according to histologic types is recorded in Table v along with their respective median survival and the number of survivals in the 15 year

Table V

RELATIONSHIP OF SURVIVAL TO HISTOLOGIC TYPES

Histologic Type	No. of Cases	Survival	
		Median (years)	15+ (years)
All Cases	377	4.0	56
L & H*			
Nodular	23	12.4	10
Diffuse	40	7.4	11
Nodular sclerosis	149	4.2	23
Mixed	97	2.5	10
Diffuse fibrosis	47	0.9	1
Reticular	21	2.3	1

* Lymphocytic and/or histiocytic.

TABLE VI

RELATIONSHIP OF HISTOLOGIC TYPES TO CLINICAL STAGES

Histologic Groups	No. of Cases	Clinical Stages					
		I		II		III	
		No.	Per Cent	No.	Per Cent	No.	Per Cent
L & H*							
Nodular	23	18	78	2	9	3	13
Diffuse	40	26	65	11	27	3	8
Nodular sclerosis	149	53	36	54	36	42	28
Mixed	97	36	37	39	40	22	23
Diffuse fibrosis	47	5	11	13	27	29	62
Reticular	21	4	19	8	38	9	43
Total	377	142	38	127	34	108	28

* Lymphocytic and/or histiocytic.

follow-up period. There is a definite relationship between histologic types and median survival with significant difference in median survival between nodular and diffuse types of L & H, between the L & H types and nodular sclerosis, and between these three types and mixed, diffuse fibrosis, and reticular types. The median survival of the L & H nodular type of 12.4 years is in remarkable contrast to all other types. The majority of survivors at 15 years, 44 of the 56 cases (79 per cent), are found within the L & H and nodular sclerosis groups. It is important to note that the largest single group of survivors, 23 of the 56 (41 per cent), exhibited the features of the nodular sclerosis type which would be classified in the granuloma group according to the criteria of Jackson and Parker.[6] Classification on the basis of the predominant histologic features into these histologic types appears to identify prognostically significant case groups that would be lost in the broad granuloma group. Comparison with the histologic types of Jackson and Parker will be presented in a subsequent section.

RELATIONSHIP OF HISTOLOGIC FEATURES TO CLINICAL STAGES

The cases of each histologic type were separated into groups according to the clinical stage observed at the time of biopsy and are summarized in Table VI. There is an apparent relationship between the L & H groups and Stage I, diffuse fibrosis and Stage III, and the reticular group and Stages II and III. The preponderance of cases (78 per cent) with the nodular L & H type and the majority (65 per cent) of the diffuse L & H type were initially observed with Stage I disease while the majority of diffuse fibrosis (62 per cent) were in Stage III. In the reticular type less than half of the cases (43 per cent) were in Stage III when first observed, but almost all the cases (81 per cent) were in Stage II and III. It appears that the histologic types characterized by lymphocytic proliferation and an infrequency of Reed-Sternberg cells are associated with Stage I while the types with lymphocytic depletion and numerous Reed-Sternberg cells are found with Stage III or Stage II and III disease.

The cases of nodular sclerosis and mixed types are rather uniformly distributed among all the stages with a distinctive tendency for the cases to present in Stages I and II. This observation emphasizes the need for lymph node biopsies from more than one region when the patient is observed in Stage II or III in order to appraise the histologic state of the individual case accurately. A difference in the histologic

Table VII

RELATIONSHIP OF HISTOLOGIC TYPES AND CLINICAL STAGES TO SURVIVAL

(Median Survival in Years)

Histologic Groups	All Stages	Clinical Stage		
		I	II	III
L & H				
Nodular	12.4	16.0	12.0	4.3
Diffuse	7.4	9.5	5.8	5.5*
Nodular sclerosis	4.2	11.0	3.2	1.8
Mixed	2.5	4.8	2.5	1.2
Diffuse fibrosis	0.9	1.1	3.2	0.4
Reticular	2.3	5.7	2.7	0.6
Total	4.0	9.1	3.2	1.3

* Only 3 cases in this group; therefore the average was used as more representative (median — 7.7).

appearance in the biopsies from this study would appear to indicate a significant change in the process. This interpretation differs from the meaningless cellular proliferation concept that invalidates attempts at classification.

The median survivals for the combined histologic and clinical stage groups are recorded in Table vii. There is a striking contrast in median survival between the L & H types in Stage i and diffuse fibrosis and reticular groups in Stage ii and iii where the majority of each type is observed. They range from 16 years in L & H nodular type in Stage i to 0.4 years for diffuse fibrosis in Stage iii. The cases of nodular sclerosis in Stage i also present a remarkably long median survival of 11 years in Stage i which is comparable to the L & H groups. In Stage ii and iii, however, the median survivals for nodular sclerosis are significantly shorter than the L & H groups and similar to those of the mixed, diffuse fibrosis, and reticular groups in Stage ii but considerably longer than those of the diffuse fibrosis and reticular groups in Stage iii. Nodular sclerosis, the most common histologic type, presents significant evidence of quiescent or very slowly progressive disease in Stage i where a major proportion of the cases (36 per cent) of the group was initially observed.

RELATIONSHIP OF SYSTEMIC SYMPTOMS AND HISTOLOGIC FEATURES TO CLINICAL STAGES

In Table viii the influence of systemic symptoms on clinical stages is related to histologic features according to 5, 10, and 15 year survivors. The previously noted significant influence of systemic symptoms on clinical Stages ii and iii in survival recorded in Table iii appears to be the result of both the frequency and the slow rate of progression of cases with nodular sclerosis in Stage ii and iii and the persistent absence of symptoms. In Stage iiA and iiiA without symptoms, 18 of the 35 cases that survived 5 years, 8 out of the 14 that lived 10 years, and 4 out of the 5 that reached 15 years were from the nodular sclerosis group. In Stage iiB and iiiB (with symptoms) only 6 of 16 surviving 5 years were from the nodular sclerosis group. The only case with symptoms surviving 10 years was from this group, but the patient failed to live 15 years. This observation provides further evidence of the tendency for slow progression with nodular sclerosis even in Stages ii and iii when systemic symptoms are absent.

RELATIONSHIP OF THE NODULAR SCLEROSING GROUP TO INVOLVEMENT OF THE MEDIASTINUM AND CLINICAL STAGE

The incidence of mediastinal involvement observed in the nodular sclerosing group and all other types combined is recorded in Table ix. These data dramatically demonstrate the significant relationship between nodular sclerosis and mediastinal involvement. Cases of the nodular sclerosing type accounted for 88 of the 149 cases (59 per cent) presenting with initial manifestation of mediastinal involvement. The difference is most remarkable in Stage i where mediastinal involvement with nodular sclerosis occurs 15 times as frequently as in all other types of Hodgkin's disease combined. In Stage ii and iii

TABLE VIII

INFLUENCE OF SYSTEMIC SYMPTOMS IN RELATIONSHIP TO CLINICAL STAGES AND HISTOLOGIC TYPES

Clinical Stages	Total Patients	Total Survivors		No. of Survivors in Each Histologic Type					
				L & H*		Nodular Sclerosis	Mixed	Diffuse Fibrosis	Reticular
		No.	Per Cent	Nod.	Diff.				
5 Yr. Survivals									
Total	377	151	40	18	28	66	30	4	5
No symptoms	219	135	62						
I	142	100	70	15	20	42	18	2	3
IIA	55	26	47	2	2	13	7	1	1
IIIA	22	9	41	1	2	5	1	0	0
With symptoms	158	16	10						
IIB	72	12	17	0	4	3	4	1	0
IIIB	86	4	5	0	0	3	0	0	1
10 Yr. Survivals									
Total	377	82	22	15	13	37	14	2	1
No symptoms	219	81	37						
I	142	67	47	13	12	29	11	1	1
IIA	55	12	22	2	0	7	2	1	0
IIIA	22	2	9	0	0	1	1	0	0
With symptoms	158	1	1						
IIB	72	1	1	0	1	0	0	0	0
IIIB	86	0	0	0	0	0	0	0	0
15 Yr. Survivals									
Total	377	56	15	10	11	23	10	1	1
No symptoms	219	56	26						
I	142	51	36	10	11	19	9	1	1
IIA	55	5	9	0	0	4	1	0	0
IIIA	22	0	0	0	0	0	0	0	0
With symptoms	158	0	0						
IIB	72	0	0	0	0	0	0	0	0
IIIB	86	0	0	0	0	0	0	0	0

* Lymphocytic and/or histiocytic.

mediastinal involvement is still numerically greater in nodular sclerosis than in all other types combined. The difference in incidence remains very significant although only approximately twice as great. Furthermore, the occurrence of mediastinal involvement in 24 cases of the nodular sclerosis type in Stage I is almost equal to the number of cases from all other groups in Stages II or III and the incidence is greater.

Table IX

COMPARISON OF FREQUENCY OF MEDIASTINAL INVOLVEMENT IN NODULAR SCLEROSIS WITH OTHER HISTOLOGIC TYPES

Clinical Stages	Nodular Sclerosis Total	Nodular Sclerosis Mediastinal Involvement No. of Cases	Nodular Sclerosis Mediastinal Involvement Per Cent	Other Types* Total	Other Types* Mediastinal Involvement No. of Cases	Other Types* Mediastinal Involvement Per Cent
I	53	24	45	89	3	3
II	54	34	63	73	26	36
III	42	30	71	66	25	38
Total	149	88	59	228	54	24

* Other types include lymphocytic and histiocytic (nodular and diffuse), mixed type, diffuse fibrosis, and reticular.

HISTOLOGIC TYPES OF JACKSON AND PARKER

Comparison study of the significance of the histologic types of Jackson and Parker, namely paragranuloma, granuloma, and sarcoma, was accomplished by parallel classification, strictly according to the ctiteria of these authors. Of the 377 cases in this study, 344 were classified as granuloma, 30 as paragranuloma, and 3 as sarcoma. Inclusion of 344 or 91 per cent of the cases in the granuloma group clearly demonstrates the lack of distinctiveness of this type and precludes effective correlation with clinical stages. It should be emphasized that included within this group are the majority of cases of the L & H diffuse type, all of the nodular sclerosis, mixed, and diffuse fibrosis types, and all but 3 cases of the reticular type. This observation clearly demonstrates the heterogenous character of the granuloma type. The median survival of the paragranuloma type is 11.2 years, granuloma 3.2 years, and sarcoma 0.6 years. Of the 56 survivors at 15 years, 44 cases were classified as granuloma and 12 as paragranuloma. It is readily apparent that this classification is effective in the identification of only a small proportion of prolonged survivors. Furthermore, the heterogenous composition of the granuloma group includes 79 per cent of the survivors and yet has a median survival of 3.2 years which closely approximates only the mixed histologic type of the present study.

CAUSE OF DEATH

The factors associated with death during the 15 to 18 year follow-up period will be discussed in detail elsewhere.[9] Of the 321 patients who died during this period 307 were dead from Hodgkin's disease and related factors. Two of the remaining 14 patients died with leukemia and 2 with bronchogenic carcinoma. The remainder were dead of a variety of causes which in-

Table X

RELATIONSHIP OF RATE OF PROGRESSION TO THE CLINICAL AND HISTOLOGIC FACTORS IN HODGKIN'S DISEASE

Type	Median Survival (Years)	Clinical Stage (Distribution)	Systemic Symptoms	Histologic Manifestations
Quiescent	9–15	I	0	L & H nodular L & H diffuse Nodular sclerosis
Changing	3–6	II and III	0	Nodular sclerosis Mixed
Progressive	0.5–1.5	II and III	+	Nodular sclerosis Mixed Diffuse fibrosis Reticular

cluded one from suicide and 2 from automobile accidents and one in a plane crash.

DISCUSSION

The demonstrated relationship between histologic types, clinical stages, and survival in this study raises important prognostic and conceptual implications. It is believed to indicate that the wide variations in the histologic findings in patients with Hodgkin's disease are manifestations of differences in responsiveness of the host rather than an expression of a mixed lymphoma as suggested by Lumb.[10] The histologic findings not only provide a basis for prognosis and evaluation of the effectiveness of therapy but a basis for the appraisal of an individual patient's status at a particular moment. When used in conjunction with the existent clinical stage, the histologic types achieve considerable significance in case evaluation.

Comparison study of the prognostic value of these histologic types with those of Jackson and Parker clearly indicates the ineffectiveness of the granuloma type, both in prognosis and in correlation with clinical stages. The paragranuloma and sarcoma types, while distinctive, are of limited value due to the small proportion of cases included with these groups.

A prognostic schema is recorded in Table x which relates the 6 new histologic types from this study with the clinical stages, systemic symptoms, and median survival. From this schema it is apparent that there are two types of Hodgkin's disease, quiescent and progressive, with an intermediate or changing form. The quiescent type with a median survival from 9 to 15 years is observed clinically in Stage I and manifested histologically by either nodular sclerosis or a proliferation of lymphocytes and/or histiocytes in either nodular or diffuse form. Progressive disease is of brief duration (0.5 to 1.5 years) and evidenced clinically by Stage II and III with systemic symptoms and histologically by diffuse fibrosis, reticular and mixed types. In general, changing disease which is evolving from quiescent to progressive in varying rates has a median survival from 3 to 6 years and is reflected by mixed or nodular sclerosis types and Stages II or III without systemic symptoms. Undoubtedly, the effectiveness of the histologic appraisal in this prognostic approach would be greatly enhanced through biopsy of lymph nodes from multiple regions in patients with clinical Stage II and III disease or of recurrent lymphadenopathy in any region in those with quiescent disease. Improvement in accuracy of clinical staging can be accomplished by use of lymphangiograms for involvement of the retroperitoneum and by careful routine search of the mediastinum roentgenologically for obscured lymphadenopathy.

From this study it is apparent that nodular sclerosis, a previously undescribed histologic type, is a regional expression of Hodgkin's disease. The incidence of mediastinal involvement in each stage exceeds all other types combined in both number and frequency. In Stage I the difference in frequency is most dramatic where it is 15 times as great as all other types combined. The prolonged median survival in Stage I in nodular sclerosis and the prominent tendency of this type to undergo spontaneous sclerosis with collagen suggest a significant relationship between the sclerosing feature of this regional lesion and quiescent disease. Nodular sclerosis in this series in Stage I assumes a role of primary importance prognostically. It represents the largest incidence of any histologic type in Stage I, exceeding the L & H types combined, and a prolonged median survival of 11 years in 19 of the 56 survivors (34 per cent). Further study on a larger series of cases is in progress in an attempt to define in detail the histologic and roentgenologic character of the process. The findings thus far do not provide support for the thymic origin of Hodgkin's disease as proposed by Thomson[19] but indicate the regional character of the nodular sclerosing type in the mediastinum and adjacent supraclavicular regions.

The general association of histologic types and clinical stages is considered to be dependent primarily upon an inverse relationship between lymphocytes and Reed-Sternberg cells. With a decrease in lymphocytes there is an increase in Reed-Sternberg cells, histiocytes, eosinophils, and the early formation of disorderly fibrosis. The latter eventually may become the predominant feature as the diffuse fibrosis type. Paralleling the decrease in lymphocytes and the increase in other histologic elements there appears to be a change from quiescent to progressive disease from Stage I to Stages II and III. This decrease in lymphocytes in progressive disease may be related to the inability to develop delayed hypersensitivity, the immunologic defect described in Hodgkin's disease by Schier *et al.*[17] It may also be a factor in the frequent absence of homograft rejection in Hodgkin's disease reported by Kelly *et al.*[8] and the basis for the lymphocytic depletion observed by Rebuck *et al.*[14] in inflammatory reactions in skin windows on patients with Hodgkin's disease. These observations support the importance of the lymphocyte in the Hodgkin's disease process as suggested by Rosenthal[16] many years ago. It further suggests that the proliferation of lymphocytes which is usually associated with Stage I disease is a favorable response of the host, and the prolonged survivals in this situation are the result of the quiescent state achieved by the host rather than effective therapy. The view that the state of the host is the determining factor is strongly supported by the almost identical survival figures in the male population of Peters and Middlemiss'[13] series and of this study, which includes patients treated by widely variable regimens in countless hospitals throughout the country.

SUMMARY

1. The relationship between histologic features, clinical stages, and survival in Hodgkin's disease is evaluated in this presentation on the basis of a morphologic study of 377 U.S. Army cases from World War II in a 15 to 18 year follow-up period.

2. A relationship is demonstrated between 5 new histologic types, the clinical stages of Peters, and survival. These histologic types appear to reflect differences in the state of the host. When used in conjunction with clinical stages, they provide an effective basis for prognosis and the evaluation of individual cases.

3. Nodular sclerosis, a histologic type characterized by the formation of collagen, is associated with a remarkably high incidence of mediastinal involvement and appears to represent a regional expression of Hodgkin's disease. It is of major prognostic importance since nodular sclerosis is the most common histologic type observed in Stage I of this study and has a median survival of 11 years.

4. Comparison study with the histologic types of Jackson and Parker reveals the prognostic ineffectiveness of this classification, primarily due to the heterogeneity of the granuloma type.

University of Southern California
School of Medicine
Department of Pathology
1200 North State Street
Los Angeles 90033, California

REFERENCES

1. Bonenfant, J. L. La lympho-réticulose médullaire chronique maligne avec syndrome Hodgkinien (paragranulome). *Bull. Assoc. franç. L'étude Cancer*, 1954, *41*, 296–315.
2. Croizat, P., Ponthus, P., Papillon, J., Revol, L., Dargent, M., Pinet, F., Kuentz, M., and Lenoble, E. Le prognostic de la maladie de Hodgkin. *Presse méd.*, 1958, *66*, 1135–1138.
3. Dubin, I. N. Poverty of immunological mechanism in patients with Hodgkin's disease. *Ann. Int. Med.*, 1947, *27*, 898–913.
4. Harrison, C. V. Benign Hodgkin's disease (Hodgkin's paragranuloma). *J. Path. & Bact.*, 1952, *64*, 513–518.
5. Hoster, H. A., Dratman, M. B., Craver, L. F., and Rolnick, H. A. Hodgkin's disease (Part I); 1832–1947. *Cancer Res.*, 1948, *8*, 1–78.
6. Jackson, H., Jr., and Parker, F., Jr. Hodgkin's Disease and Allied Disorders. Oxford University Press, New York, 1947.
7. Jelliffe, A. M., and Thomson, A. D. Prognosis in Hodgkin's disease. *Brit. J. Cancer*, 1955, *9*, 21–36.

8. Kelly, W. D., Lamb, D. L., Varco, R. L., and Good, R. A. Investigation of Hodgkin's disease with respect to problem of homotransplantation. *Ann. New York Acad. Sc.*, 1960, *87*, 187–202.
9. Lukes, R. J., Butler, J. J., and Hicks, E. Hodgkin's disease: evaluation of significance of clinical stages and histologic findings on basis of 377 U. S. Army cases from World War II (1942–1945). To be published.
10. Lumb, G. D. Tumours of Lymphoid Tissue. E. & S. Livingstone, Ltd., Edinburgh, 1954.
11. Lumb, G., and Newton, K. A. Prognosis in tumors of lymphoid tissue; analysis of 602 cases. *Cancer*, 1957, *10*, 976–993.
12. Peters, M. V. Study of survivals in Hodgkin's disease treated radiologically. Am. J. Roentgenol. & Rad. Therapy, 1950, *63*, 299–311.
13. Peters, M. V., and Middlemiss, K. C. H. Study of Hodgkin's disease treated by irradiation. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1958, *79*, 114–121.
14. Rebuck, J. W., Monto, R. W., Monaghan, E. A., and Riddle, J. M. Potentialities of lymphocyte, with additional reference to its dysfunction in Hodgkin's disease. *Ann. New York Acad. Sc.*, 1958, *73*, 8–38.
15. Robb-Smith, A. H. T. Reticulosis and reticulosarcoma; histological classification. *J. Path. & Bact.*, 1938, *47*, 457–480.
16. Rosenthal, S. R. Significance of tissue lymphocytes in prognosis of lymphogranulomatosis. *A.M.A. Arch. Path.*, 1936, *21*, 628–646.
17. Schier, W. W., Roth, A., Ostroff, G., and Schrift, M. H. Hodgkin's disease and immunity. *Am. J. Med.*, 1956, *20*, 94–99.
18. Smetana, H. F., and Cohen, B. M. Mortality in relation to histologic type in Hodgkin's disease. *Blood*, 1956, *11*, 211–224.
19. Thomson, A. D. Thymic origin of Hodgkin's disease. *Brit. J. Cancer*, 1955, *9*, 37–50.
20. Winterhalter, K. H. Verlauf und Prognose der Lymphogranulomatose anhand von 140 Fällen. Doctoral Dissertation. Juris-Verlag, Zürich, 1961.
21. Wright, C. J. E. Hodgkin's paragranuloma. *Cancer*, 1956, *9*, 773–777.

THE CONTRIBUTION OF RADIATION THERAPY IN THE CONTROL OF EARLY LYMPHOMAS*

By M. VERA PETERS, M.D.
TORONTO, ONTARIO, CANADA

THE lymphomas comprise a group of malignant disorders of lymphoid and reticulum cells. The primitive mesenchymal stem cells are generally accepted by pathologists as possessing the potential to differentiate into any of the cell types characteristic of the classic or mixed histologic pictures of the lymphomas. Transitions from one type to another may be observed. This variety of clinical pictures provides a continuous challenge for the clinician, unequalled by any other malignancy.

This paper concerns only the reticulum cell sarcomas, giant follicular lymphomas and lymphosarcomas. From 1934 until 1952 standard radiation therapy methods were employed for the group of malignant lymphomas in the Ontario Cancer Institute, Toronto, formerly the Department of Radiotherapy, Toronto General Hospital. Included in this study are only the 414 patients presenting up to 1952 to allow a minimum of ten years for follow-up.

This study was intended as a critical analysis of treatment methods but has been rewarding in other respects. It has established the responses and the survival rates following a fairly aggressive irradiation, with many management variables. It has provided further evidence on the controversial subject of the wisdom of or necessity for any form of treatment for the symptom free lymphoma patient. The survey has revealed a very simple clinical classification for this group of lymphomas. The group is reported in its entirety for some relationships and for others it is divided into the three main morphologic types: reticulum cell sarcoma, giant follicular lymphoma and lymphosarcoma. An attempt has been made to determine a useful radiotherapeutic approach in each stage of the disease.

HISTORICAL CONSIDERATIONS

A historical review is beyond the scope of this paper but any published review would be remiss without giving due credit to the pathologists who originally described the lymphomas. Virchow,[31] in 1863, Kundrat,[14] in 1893, and Paltauf,[21] in 1896, described these tumors of lymphoid origin, which have recently acquired the title of lymphomas. The works of Ewing,[6] in 1913, Oberling,[19] in 1928, and Roulet,[26] in 1930, are important for the description and the separation of the reticulum cell sarcoma from the main group of lymphomas. Credit for the recognition of the giant follicular lymphomas is given to Brill, Baehr, and Rosenthal[3] whose study was reported in 1925. Symmers[30] later supported their findings. Many years previously Wilks[32] identified Hodgkin's disease as a separate entity in the over-all group of lymphoreticulo-endothelial malignancies. One cannot refer to Hodgkin's disease without mentioning other pathologists of fame, Greenfield,[9] Sternberg,[28] and Reed,[24] who made special contributions to its true identity.

SCOPE OF STUDY

In this presentation, detailed data on Hodgkin's disease have been omitted but some comparative references will be made to previous publications[22,23] in which our experiences with this disease have been covered. An analysis has been prepared of all the patients with pathologically proven lymphoma who were admitted to this Institute for treatment from 1934 to 1952, inclusive The Chief in Pathology, Dr. T. C. Brown, has reviewed and has concurred in the histologic diagnosis in those cases surviving more than 10 years.

---

* Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1-4, 1963. Part of the Symposium: Lymphomas; Chairman, Dr. James J. Nickson, New York, New York.

Table I

CLASSIFICATION OF THE LYMPHOMAS (EXCLUDING HODGKIN'S DISEASE)

I. Single lymph node region,
or single site in extranodal tissue

II. Multiple lymph node regions,
or single extranodal site with involvement of adjacent lymphatic region

III. Evidence of systemic disease,
or involvement of liver, spleen, or bone marrow,
or single extranodal site with involvement of remote lymphatic region.

A close scrutiny of the clinical course of this group of lymphomas in relation to the extent and sites of involvement on first admission for treatment suggested the classification shown in Table I.

THE PLAN OF MANAGEMENT IN THIS SERIES

The previous plan of management as employed in this series was designed by the late Dr. G. E. Richards, former chief in Radiotherapy. The radiation dosage applied depended on the site and extent of involvement and the radiosensitivity demonstrated during the treatment. All tumor doses quoted have been calculated during the preparation of this paper and are thus subject to errors as the anteroposterior diameter of each patient was not recorded. Sites of minimal involvement of the more radiosensitive tumors received a single incident dose of 800 r–1,000 r, repeated in 2 months. More extensive involvement of a single region received a tumor dose within the range of 1,500 rads in 1 week to a high of 4,000 rads in 3–5 weeks. The reticulum cell sarcomas and the more radioresistant lymphosarcomas received a higher tumor dose within the range of 4,000 rads in 4 weeks to 6,500 rads in 6 weeks. Similar tumor dose levels were employed for the treatment of localized recurrences in sites not previously irradiated.

In addition, during the entire period studied, more than 50 per cent of this series received prophylactic irradiation consisting of 2 or 3 courses of treatment to all the uninvolved main lymphatic chains, with an interval of 2 months between courses. During each course each of the uninvolved lymphatic regions (both peripheral and central) received a tumor dose of 600 rads to 800 rads.

From 1934 to 1938 a 200 kv. unit with a half value layer of 1.5 mm. Cu was employed for local irradiation. But from 1938 to 1952 the majority of patients were treated using a 400 kv. apparatus with a half value layer of 3.5 mm. Cu. The treatment plan was very similar to that reported by Fuller and Fletcher[7] in 1962.

There were, of course, a multitude of variables throughout this series but the over-all plan was attempted if not always completed. The total dosage of any area was altered according to the volume of tissue to be irradiated. Radical surgery or local excisions preceding irradiation provided another variable in a minority of the cases and this divergence will be considered.

As recommended by Osgood,[20] the crude survival rates from the year of admission include a 3 month and a 6 month survival summation in addition to the yearly survival up to 20 years and are shown in Table II. A summary of Table II is presented in Table III showing the percentage surviving at the more crucial intervals. The discouraging note is the 1 year survival rate of only 50 per cent. Thus one half of the total number in this series died within 1 year of treatment. An additional one-quarter (26 per cent) of the total number expired between 1 and 5 years. After 5 years following admission, the drop in survival rate was more gradual. Only 10 per cent succumbed between 5 and 15 years after treatment. The long term crude survival rates are comparable to those published by Cook *et al.*,[3] who report a 12.5 per cent 15 year survival out of 191 cases and an 11.2 per cent 20 year survival out of 133 cases. The present series reveals a 14 per cent 15 year survival rate and a 9 per cent 20 year survival rate.

The 5, 10 and 15 year survivals related

TABLE II

LYMPHOMAS—TOTAL SERIES SURVIVALS BY YEAR OF ADMISSION

Year	No. of Cases	3 mo.	6 mo.	1 yr.	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1934	10	9	9	9	7	6	5	5	5	4	4	4	4	4	4	3	3	3	2	2	2	2	2
1935	9	8	8	6	4	4	3	1	—														
1936	9	9	7	4	4	4	3	1	—														
1937	13	12	8	7	5	4	4	3	3	3	3	3	3	2	2	2	2	2	2	2	1	1	1
1938	15	11	10	6	5	4	3	3	3	3	3	3	3	3	3	2	2	2	2	2	2	2	2
1939	10	9	7	6	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
1940	11	9	6	5	3	2	1	1	1	1	1	—											
1941	17	14	12	11	10	7	7	7	6	6	6	6	6	5	5	5	5	4	2	1	1	1	1
1942	20	15	11	7	4	4	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
1943	9	7	7	6	6	6	6	6	6	6	5	5	5	5	5	5	5	5	4	4	4	4	
1944	16	13	10	9	9	7	7	5	5	5	5	4	4	3	2	2	2	2	2	2	2		
1945	41	23	18	12	10	8	6	6	4	4	3	3	3	3	3	3	3	3	3	3			
1946	19	16	14	10	10	8	8	8	6	6	6	6	6	6	6	6	4	4	4				
1947	30	24	23	20	16	15	10	10	10	10	9	9	8	6	5	5	4	3					
1948	27	18	12	9	8	5	5	5	4	3	2	2	2	2	1	1	—						
1949	33	25	20	17	14	10	9	6	6	5	5	5	5	4	3	2							
1950	42	27	21	17	11	9	9	8	7	6	5	5	5	5	5								
1951	38	30	28	25	17	13	10	8	8	7	6	5	5	5									
1952	45	37	28	22	20	16	13	12	11	7	7	7	6										
Total No. Cases	414	316	259	208	166	134	114	99	89	80	74	71	69	57	43	40	34	32	25	20	16	14	10
Per Cent		76	63	50	40	32	27	24	21	19	18	17	17	15	14	14	13	14	13	11	12	11	9

to both sex and age are shown in Table IV which also supplies detailed information on the completeness of follow-up and causes of death. As reported by many authors,[3,4,17,18,25] there was a much higher incidence of these lymphomas in the male sex. The ratio of male to female in total numbers was almost 2 to 1. No difference in any of the comparative survival rates according to sex was found.

The age distribution was of interest. Table V shows the distribution by double decades. But when the numbers are divided according to single decades, the incidence in this series showed a steady rise from a low of 15 cases in the first decade to a high of 98 cases in the sixth decade. It was maintained at a high level in the seventh decade (81 cases) dropping to 41 cases in the eighth decade. A steady rise in incidence with increasing age would most likely be found if these figures had been corrected for total population per age group.

The most satisfactory 5, 10 and 15 year survival rates were noted in the 20 to 39 age group (Table V). In this group of 75 cases the 5 year survival rate of 39 per cent and the 10 year survival rate of 35 per cent are much higher than the corresponding rates in the total series. Less notable but still better than the average were the rates found in the 40 to 59 age group as shown in this table. Under 30 and over 60 years of

TABLE III

LYMPHOMAS—TOTAL SERIES

1, 2, 3, 5, 10, 15 AND 20 YEAR CRUDE SURVIVAL RATES

Survival (years)	Years Included	Total No.	No. Surviving	Per Cent Surviving
1	1934–1952	414	208	50
2	1934–1952	414	166	40
3	1934–1952	414	134	32
5	1934–1952	414	99	24
10	1934–1952	414	69	17
15	1934–1947	229	32	14
20	1934–1942	114	10	9

age the survival rates were considerably lower than the rates found in the total series. The number of children in this series was small. More comprehensive studies of the results of treatment of lymphomas in children were published by Bailey *et al.*[1] and by Dargeon[6] in 1961.

The survival rates were next related to the stage of disease on first admission, according to the classification cited (Table VI). Approximately one-half of those presenting in Stage I, with clinical involvement of only one site, lived 5 years. The Stage I survival rate of 36 per cent at 15 years was gratifying. In Stage II slightly less than one-quarter of the 174 cases survived 5 years and a few of these lived 10 or 15 years but the proportion was small. Only 1 patient classified as Stage III on admission lived 10 years and this particular patient expired 12 years after admission.

The comparative results according to histologic type are presented in Table VII. The reticulum cell sarcomas had a median survival of 7.9 months. Thus more than half in this series expired in less than a year and the mortality rate was still high from 1 to 2 years. In spite of the poor survival rate in the reticulum cell sarcomas, 11 Stage I patients who presented for treatment survived for at least 10 years and with 1 exception are still alive without disease. These are being followed with interest.

The giant follicular lymphomas are fewest in number but have the best survival rates. Forty-six per cent in this series survived 5 years and 24 per cent for 10 years. The median survival was 42 months.

The "unspecified" lymphomas have been combined with the lymphosarcomas because of the similarity in their clinical course and because the pathologic reviews have so far placed them in this group. More than one-half of the combined group of lymphosarcomas expired within 2 years. The drop in survival rate was gradual up to 10 years. Forty-nine patients (16 per cent) were still alive at 10 years.

The crude 5 and 10 year survival rates for the entire series have been added to

TABLE IV

LYMPHOMAS—TOTAL SERIES

5, 10, AND 15 YR. SURVIVALS RELATED TO SEX AND AGE

Age Group	5 Year									
	No. of Cases		A.		D.D.		DED.		Lost	
	M	F	M	F	M	F	M	F	M	F
0–19	24	13	4	2	20	11	—	—	—	—
20–39	52	23	21	8	27	14	—	—	4	1
40–59	105	68	27	20	71	47	4	1	3	—
60+	84	38	11	4	66	29	4	4	3	1
Not Stated	3	4	1	1	2	2	—	—	—	1
Total	268	146	64	35	186	103	8	5	10	3
			99							

Age Group	10 Year									
	No. of Cases		A.		D.D.		DED.		Lost	
	M	F	M	F	M	F	M	F	M	F
0–19	24	13	4	2	20	11	—	—	—	—
20–39	52	23	19	7	27	15	—	—	6	1
40–59	105	68	17	14	80	53	4	1	4	—
60+	84	38	5	1	70	30	5	5	4	2
Not Stated	3	3	—	—	2	2	—	1	1	1
Total	268	146	45	24	199	111	9	7	15	4
			69							

Age Group	15 Year									
	No. of Cases		A.		D.D.		DED.		Lost	
	M	F	M	F	M	F	M	F	M	F
0–19	17	7	2	1	14	6	—	—	1	—
20–39	32	16	10	4	17	11	—	—	5	1
40–59	57	34	8	5	43	29	3	—	3	—
60+	42	19	2	—	36	15	1	3	3	1
Not Stated	3	2	—	—	2	1	—	—	1	1
Total	151	78	22	10	112	62	4	3	13	3
			32							

Note: A. = alive; D.D. = died of disease; DED. = died of extraneous disease.

Table V

LYMPHOMAS—TOTAL SERIES
SURVIVAL RATES RELATED TO AGE DISTRIBUTION

Age Group	5 Year		10 Year		15 Year	
	No. of Cases	Per Cent Survival	No. of Cases	Per Cent Survival	No. of Cases	Per Cent Survival
0–19	37	16	37	16	24	12
20–39	75	39	75	35	48	29
40–59	173	27	173	18	91	14
60+	122	12	122	5	61	3
Not Stated	7	—	7	—	5	—
Total Series	414	23.9	414	16.6	229	14

those of previously published reports by other authors and are shown in Table VIII.

OPTIMUM TUMOR DOSE RANGE FOR SITES OF INVOLVEMENT

The tumor dose range of treatment which was successful in preventing a recurrence in the same site was tabulated. This information was taken only from the records of cases which survived at least 6 months, or long enough to allow a recurrence in the same site, thus precluding a large number in Stage II and most of the cases in Stage III. This was found to be (1) for giant follicular lymphoma, 2,500 rads in 2 weeks to 3,000 rads in 4 weeks; (2) for lymphosarcoma, 1,500 rads in 1 week to 4,500 rads in 4 weeks; and (3) for reticulum cell sarcoma, 5,000 rads in 4 weeks.

The wide range of successful treatment of localized lymphomas indicates the extreme differences in their radiocurability. The lymphocytic lymphosarcomas were noted to be the most radiosensitive; the presenting mass often resolved following 2 or 3 treatments of average daily dose. The apparently radiosensitive reticulum cell sarcomas did not prove to be radiocurable and a high degree of sensitivity to irradiation seemed to indicate a poor prognosis in this histologic type.

Table VI

LYMPHOMAS—TOTAL SERIES
SURVIVAL RATES ACCORDING TO STAGE

Stage	No. of Cases	Per Cent Survival		No. of Cases	Per Cent Survival
		5 Year	10 Year		15 Year
I	102	51	43	58	36
II	174	23	14	97	11
III	138	5	0.7	74	—
Total	414	24	17	229	14

TABLE VII

LYMPHOMAS—TOTAL SERIES
SURVIVAL RATES ACCORDING TO HISTOLOGIC TYPE
5, 10 AND 15 YEAR RATES AND MEDIAN SURVIVALS

Histology	Median Survivals (mo.)	Total No.	Survival		Total No.	Survival
			5 Year (per cent)	10 Year (per cent)		15 Year (per cent)
Reticulum Cell Sarcoma	7.9	75	16	15	28	— (4 cases)
Giant Follicular Lymphoma	42	37	46	24	17	— (5 cases)
Lymphosarcoma	11.4	215	25	19	132	15
Unspecified Lymphoma	16.8	87	19	10	52	6
Total	12	414	24	17	229	14

THE VALUE OF PROPHYLACTIC IRRADIATION

The courses of treatment to the uninvolved areas seemed on first review to be useful for some and not for others, when examining the individual case histories. But on a comparative assessment with groups of cases which did not receive the added treatment, no significant difference in the course of the disease or in the survival rates could be determined. For example, in a study of the giant follicular lymphoma series, where one would expect the most gratifying yield from irradiation to the uninvolved sites, 13 of 24 patients who received "prophylactic" treatment survived 5 years or more and 6 of 12 patients who received treatment only to the sites of involvement survived 5 years.

Applying the comparison to Stage 1 only, there were similar unexpected findings. In the Stage 1 lymphosarcomas for instance, 50 per cent treated by each method survived 5 years.

The most striking example of the complete lack of any advantage from "pro-

TABLE VIII

COMPARATIVE RESULTS IN THE TREATMENT OF MALIGNANT LYMPHOMAS

Authors	5 Year Survival		10 Year Survival	
	No. of Cases	Per Cent	No. of Cases	Per Cent
Craver,[4] 1947	308	26.3		
Stout,[29] 1947	119	23.5		13.4
Hare, Mulry, and Sornberger,[10] 1948	181	28.7		
Lenz, Wells, and Stout,[15] 1950	242	27.0	172	17.0
Nice, and Stenstrom,[17] 1951	132	18.9		
Nichols, Phillips, and Sommer,[18] 1957	71	25.5	43	14.0
Cook, Krabbenhoft, and Leucutia,[3] 1960	402	26.5	280	20.0
Rosenberg, Diamond, Jaslowitz, and Craver,[25] 1961	1,269	28.4		
Hilton, and Sutton,[11] 1962	65	29.0		
Peters (present series),1963	415	26.0	415	16.0

phylactic" irradiation appeared in the reticulum cell sarcomas. Only 2 of the total of 11 cases which survived more than 10 years received additional treatment to the uninvolved areas.

It is felt from our past experience that there is no merit in treating the lymphatics not clinically involved, even in the earliest stage of the lymphomas of the three types studied. This decision is contrary to the report in 1961 of Holme and Kunkler.[12] This was surprising indeed, in view of the value of "prophylactic" irradiation which which has apparently been demonstrated by our previous experience[22,23] in Hodgkin's disease.

CONTRIBUTION OF SURGERY

The third variable which applied to 20 per cent of the total series was the influence of surgery as an integral part of the initial management. All the postoperative patients in the series received radiation therapy to the site of involvement.

A total of 84 cases had previous surgical procedures but only 11 were performed for involvement of the peripheral lymphatic regions. The remaining 73 were recorded as excisions of extranodal or visceral primary sites. Surgery was performed chiefly as a means of establishing the diagnosis and the more radical procedures were often carried out when other disease was suspected. For lesions of the gastrointestinal tract, a surgical excision is the preferable method of treatment. But it was difficult to demonstrate a superiority of one type of treatment over the other for sites which were suitable for either treatment. In fact, in a comparative study of the Stage 1 lymphomas according to method of treatment, 29 or 52 per cent of a total of 56 patients treated by irradiation alone survived 5 years and 22 or 43 per cent of a total of 46 patients survived 5 years when treated by surgery and postoperative radiation.

The author has had no personal experience with surgery as the sole method of treatment in Stage 1 cases. Smith and Klopp[17] presented their surgical experience in 1961. The earlier advocates of the surgical approach include Jackson and Parker[13] in 1947 and Gall and Mallory[8] in 1942. Lumb's review[16] in 1954 adds further support to this method of treatment for some sites of involvement.

DISCUSSION

The results of active treatment of the lymphomas in this series have been presented and the preferable methods of treatment as derived from this series have been clarified. However, one is still faced with the problem of deciding whether or not there is any merit in active treatment for the patient who presents without symptoms. Has active treatment altered the expected survival in this series?

The effectiveness of treatment may be illustrated by graphic methods. The survival curves plotted on semilog paper are shown in Figures 1 through 4. In each graph the survival curve of the lymphoma group is compared with a survival curve of the

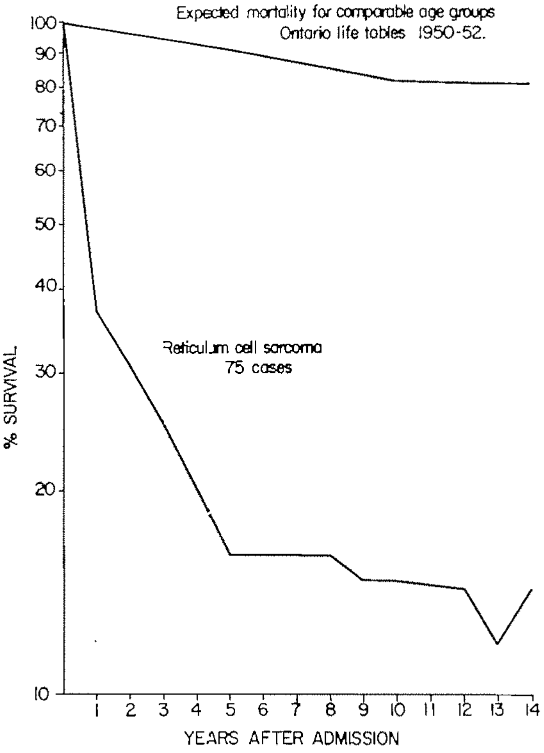


Fig. 1.

normal population compiled from the life tables of the Province of Ontario for 1950 to 1952 and adjusted so as to correspond to the age distribution of the patients studied.

Regardless of the histologic type the survival curve of the lymphoma population drops much more rapidly than that of the control population up to 10 years, after which the curve assumes a line more nearly parallel to that of the whole population. Thus the survivors beyond 10 years have a life expectancy approaching that of the population as a whole.

The assumption that the 69 patients who survived 10 years were "true lymphomas" has been made as a result of the concurrence of 2 or more senior pathologists. On this premise, one can accept the likelihood that some patients have been cured by radiation therapy, and that others have had their life expectancy changed to permit them to share the same risks as the entire population of the same ages.

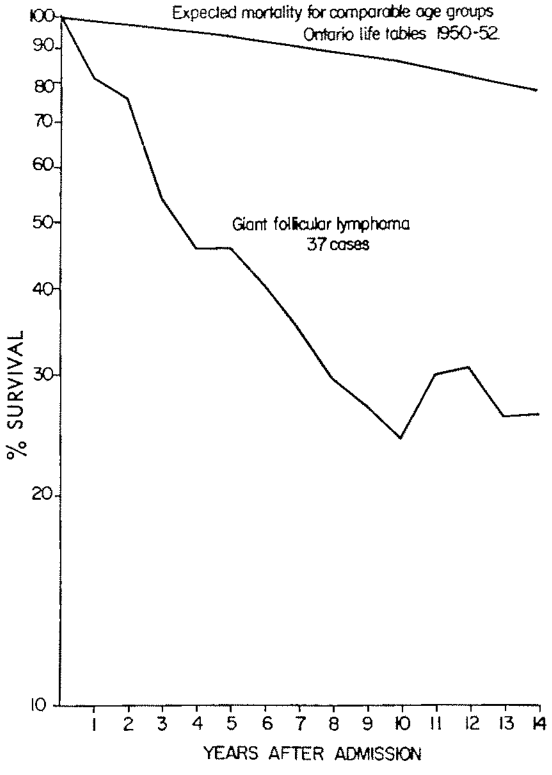


Fig. 2.

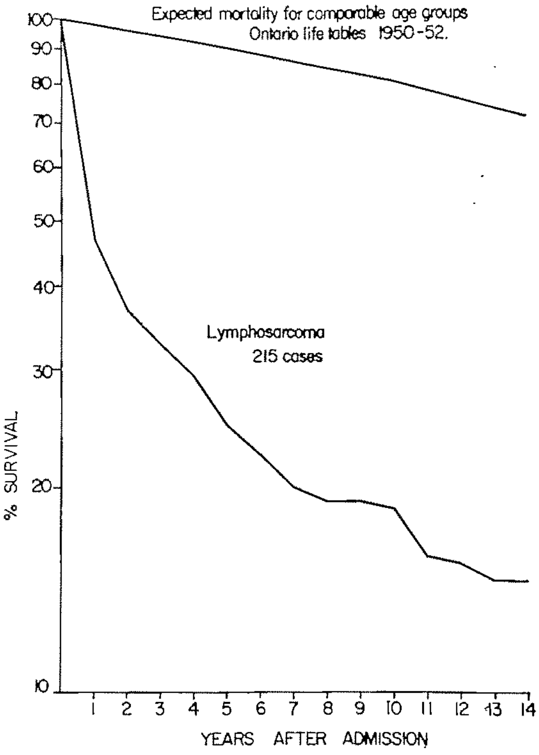


Fig. 3.

The up-to-date follow-up on these 69 patients is in agreement with this interpretation of the survival graphs. It is of interest to find that 51 patients are still alive and 42 of these still have a recurrent-free record and their life span since admission varies from 10 to 28 years. The remaining 9 survivors are still well but have had suspected recurrences treated in the interval. Extraneous disease has been the cause of death in 4 patients who were free of disease prior to death and 14 have expired as a result of the disease.

If one considers only the 42 patients still living who have had no recurrences to date, one finds that 31 of these patients were classified as Stage I on admission. The remaining 11 patients were classed Stage II but some of these might have been classed Stage I if all the necessary details had been recorded. They were placed in Stage II because there was mention of enlarged lymph nodes distant to the primary site in their case histories, but the miminal irradiation

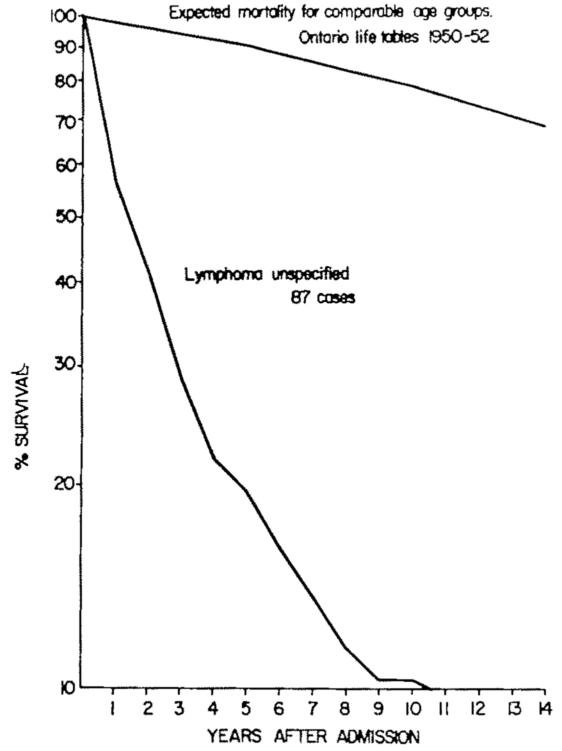


Fig. 4.

applied to these additional sites suggests that the suspected involvement might not have been significant.

Disregarding the possible errors in a retrospective study, if one expresses these numbers as a proportion of the total numbers admitted in the corresponding stages, one finds that 30 per cent of the Stage I patients and 7 per cent of the Stage II patients are still free of disease. Because of the small number of patients in Stage II who have a clear record to date and because of the doubt surrounding their classification, I would be unwilling to intimate a real hope for cure in this stage as a result of active treatment on the premise of this study. Incidentally, in this respect Hodgkin's disease is conspicuously unlike the other lymphomas because of the better than average long term survival rates in the group presenting for treatment with involvement of two or more contiguous lymphatic regions.[23]

But one can make more valid deductions in Stage I lymphomas because of the significantly larger percentage of recurrent free survivors. The survival rate in Stage I strengthens the hypothesis that the lymphomas in this group are unicentric in origin and allows more promising speculation. The unexpected discovery that the good responses are just as frequent when no treatment is directed to any of the lymphatics beyond the primary involvement adds support to this theory. If one accepts the likelihood of an unicentric origin, there must be merit in advising active treatment for the symptom free lymphoma patient in Stage I. The decision to treat, or not to treat, could only be decided by a properly controlled prospective parallel series comparing active treatment on first diagnosis with the close watch policy and symptomatic treatment. But the accumulating evidence that the lymphomas are unicentric in origin suggests that a randomized series including Stage I might deprive many patients of a chance for a cure. In Stage II, however, there is no concrete evidence that controlled trials might entail a risk to any patient in the absence of symptoms.

Further evidence that aggressive treatment in Stage I can undoubtedly prolong life was found in isolated case histories of patients whose local disease threatened their immediate survival. The prime example in this series was a female patient, aged 36, who had a reticulum cell sarcoma of the mediastinum, pathologically proven at thoracotomy, and who presented with clinical evidence of acute superior vena caval obstruction. She received a calculated tumor dose of 4,000 rads in 4 weeks to the mediastinum only, using a 400 kv. unit, and is alive 10 years later, having had no recurrence in the interval.

Three patients in this series who presented with cord compression due to extradural lymphosarcoma lived more than 15 years. One has expired since, but 2 are still well 15 and 19 years after treatment. Each of these patients received a tumor dose of approximately 3,500 rads to the level of involvement following a decompression laminectomy.

Our experience with aggressive treatment in Stage III has been extremely poor. One gets the impression that the survivals in this stage were shortened by radical irradiation. Perhaps irradiation in this stage had a detrimental effect on the patient's immune mechanisms. It was my experience that overzealous treatment in the advanced stage contributed to the low median survival of 1 year in this total series. Fortunately, chemotherapy has relieved the pressure from radiation therapy in the advanced stage. No doubt, the volume of patients in this stage and the inclusion of all cases, whether or not any treatment was given, have also influenced the median survival.

The discussion of the role of radiation therapy would not be complete without some mention of the treatment of local recurrences. Following worthwhile remissions, radical irradiation of single sites of involvement has been successful in providing further remissions in both lymphosarcoma and giant follicular lymphoma. The response one would expect with a steady decline in the length of successive remissions was not typical in these two cytologic types. More often the disease seemed to advance at a steady pace until the preterminal phase. It was enlightening to find that the response to treatment of recurrent disease in reticulum cell sarcoma was strangely different. Almost invariably, the first recurrence even after a lengthy remission ushered in a more acute phase, precluding a worthwhile second remission.

Before concluding, an explanation of the departure from the treatment plan advised in cases of Hodgkin's disease in previous publications[22,23] is in order. For this group of lymphomas, the lack of any advantage resulting from "prophylactic" irradiation of uninvolved areas has been demonstrated. The author is still convinced that the additional treatment to the adjacent lymphatic regions is worthwhile in Hodgkin's disease and a controlled series, which may or may not verify the wisdom of the extra treatment, has been instituted in our hospital. In a study of the sites of successive recurrences in each histologic type, one notes that Hodgkin's disease is the only lymphoma which fairly consistently spreads by direct lymphatic extension as long as the disease remains chronic. In the other lymphomas one cannot anticipate the site of the next recurrence. Thus the difference in the plan of treatment reflects the difference in the pattern of recurrences.

CONCLUSIONS

From this study one concludes that some lymphoma patients may have been cured by adequate radiation therapy or may have had their life expectancy changed to allow them to be included with and share the same risks as the entire population of comparable age.

An appraisal of treatment methods employed in this series permits the inference that "prophylactic" irradiation of uninvolved lymphatic chains does not offer the patient any advantages.

There is harmonious disagreement among pathologists and clinicians alike on the focus of origin in this group of lymphomas. The experience related here merely adds to the documented evidence[8,13,16,27,32] in favor of an unicentric origin. As long as the disease remains confined to the site of origin, the lymphoma patient may be potentially curable. But the patient with Hodgkin's disease is likely to be potentially curable beyond this stage because of the mode of spread.

SUMMARY

1. This paper presents our experience with 414 successive patients who had histopathologically verified lymphomas (excluding Hodgkin's disease) and who were admitted to the Ontario Cancer Institute, Toronto, from 1934–1952 inclusive.

2. The clinical classification employed

was the outcome of a preliminary study relating the course of the disease to the extent of disease prior to treatment.

3. The plan of treatment employed for this series is presented and all the variables are discussed.

4. The analysis reveals the following crude survival rates from the time of admission: 1 year, 50 per cent; 5 years, 24 per cent; 10 years, 17 per cent; 15 years, 14 per cent; and 20 years, 9 per cent.

5. Relating the age of patient to prognosis, the 20 to 40 age group showed the most satisfactory survival rates.

6. The 15 year survival rate according to the clinical stage on admission of 36 per cent in Stage I, 11 per cent in Stage II, and 0 per cent in Stage III suggests the possible value of active treatment in this series.

7. The comparative results according to histologic type are presented. The following are the median survivals: reticulum cell sarcoma, 7.9 months; giant follicular lymphoma, 42 months; lymphosarcoma, 11.4 months; and lymphoma (unspecified), 16.8 months.

8. The optimum tumor dose range employed in each of the histologic types of lymphomas in this series is tabulated. A wide range of radiocurability in each type is suggested.

9. "Prophylactic" irradiation of areas not known to be involved was not found to be of any value in this series.

10. The contribution of surgery was most notable in lymphomatous lesions of the gastrointestinal tract, but, for sites of involvement which could be treated by either surgical excision or irradiation, a slight advantage was found when the treatment was irradiation alone.

11. The effectiveness of treatment in this series has been illustrated graphically, comparing the survival rate of the lymphoma population with the survival rate of the entire population of comparable age.

12. The present status of the 69 patients alive after 10 years is reported.

13. The evidence in this series that lymphomas may have an unicentric origin is documented.

14. It is suggested that prospective controlled studies in symptom free Stage II lymphoma patients are desirable in order to decide whether or not these patients benefit from active therapy.

15. The departure from the treatment plan advised for Hodgkin's disease is explained by a difference in the pattern of recurrences and the more optimistic outlook for the patient with Hodgkin's disease involving 2 or 3 adjacent lymphatic regions.

Ontario Cancer Institute
500 Sherbourne Street
Toronto 5, Ontario, Canada

I would like to especially thank Dr. D. M. Whitelaw, chief physician, Ontario Cancer Institute, for his interest and helpful guidance as well as for the preparation of the graphs, and Dr. T. C. Brown, chief pathologist. Both of these contributions have added significance to this paper. Others to whom I am indebted and wish to express my sincere thanks include Mrs. Shirley Gordon, Miss Mary McCartney and Miss Jocelyn Palm of the medical records staff; Mrs. T. Crawley, librarian; Miss Marilyn Watson, stenographer; and the photography staff.

REFERENCES

1. Bailey, R. J., Jr., Burgert, E. O., Jr., and Dahlin, D. C. Malignant lymphoma in children. *Pediatrics*, 1961, *28*, 985–992.
2. Brill, N. E., Baehr, G., and Rosenthal, N. Generalized giant lymph follicle hyperplasia of lymph nodes and spleen. *J.A.M.A.*, 1925, *84*, 668–671.
3. Cook, J. C., Krabbenhoft, K. L., and Leucutia, T. Lymphosarcoma, reticulum cell sarcoma and giant follicular lymphoma; long term results following radiation therapy. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1960, *84*, 656–665.
4. Craver, L. F. Lymphomas and leukemias. *Bull. New York Acad. Med.*, 1947, *23*, 79–100.
5. Dargeon, H. W. Lymphosarcoma in childhood. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1961, *85*, 729–732.
6. Ewing, J. Endothelioma of lymph nodes. *J. Med. Res.*, 1913, *28*, 1–39.
7. Fuller, L. M., and Fletcher, G. H. Radiotherapeutic management of lymphomatous

diseases. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *88*, 909–923.

8. Gall, E. A., and Mallory, T. B. Malignant lymphoma; clinico-pathologic survey of 618 cases. *Am. J. Path.*, 1942, *18*, 381–429.
9. Greenfield, W. S. Specimens illustrative of pathology of lymphadenoma and leucocythaemia. *Tr. Path. Soc. London*, 1878, *29*, 272–304.
10. Hare, H. F., Mulry, W. C., and Sornberger, C. F. Lymphoid tumors. *Radiology*, 1948, *50*, 506–512.
11. Hilton, G., and Sutton, P. M. Malignant lymphomas: classification, prognosis, and treatment. *Lancet*, 1962, *1*, 283–287.
12. Holme, G. M., and Kunkler, P. B. Treatment of reticuloses by chemotherapy and radiotherapy. *Brit. J. Radiol.*, 1961, *34*, 569–573.
13. Jackson, H., Jr., and Parker, F., Jr. Hodgkin's Disease and Allied Disorders. Oxford University Press, New York, 1947.
14. Kundrat, H. Ueber Lympho-sarcomatosis. *Wien. klin. Wchnschr.*, 1893, *6*, 211–234.
15. Lenz, M., Wells, J., and Stout, A. P. Hodgkin's disease and lymphosarcoma. In: Clinical Therapeutic Radiology. U. V. Portmann, editor. Thos. Nelson & Sons, New York, 1950, pp. 545–570.
16. Lumb, G. D. Tumours of Lymphoid Tissue. E. & S. Livingstone, Ltd., Edinburgh, 1954.
17. Nice, C. M., and Stenstrom, K. W. Treatment of lymphosarcoma. *Bull. Univ. Minn. Hospitals & Minn. Foundation*, 1951, *22*, 420–428.
18. Nichols, D., Phillips, C., and Sommer, A. W. Lymphosarcoma, study of five year survivals with x-ray therapy. *Texas J. Med.*, 1957, *53*, 28–34.
19. Oberling, C. Les réticulosarcomes et les réticuloendothéliosarcomes de la moëlle osseuse (sarcomes d'Ewing). *Bull. Assoc. franç. l'étude Canc.*, 1928, *17*, 259–296.
20. Osgood, E. E. Methods for analysing survival data, illustrated by Hodgkin's disease. *Am. J. Med.*, 1958, *34*, 40–47.
21. Paltauf, R. Lymphosarkom (Lymphosarkomatose, Pseudoleukämie, Myelom, Chlorom). *Ergebn. Allg. Path.*, 1896, *3*, 652–691.
22. Peters, M. V. Study of survivals in Hodgkin's disease treated radiologically. Am. J. Roentgenol. & Rad. Therapy, 1950, *63*, 299–311.
23. Peters, M. V., and Middlemiss, K. C. H. Study of Hodgkin's disease treated by irradiation. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1958, *79*, 114–121.
24. Reed, D. M. On pathological changes in Hodgkin's disease, with especial reference to its relation to tuberculosis. *Johns Hopkins Hosp. Rep.*, 1902, *10*, 133–196.
25. Rosenberg, S. A., Diamond, H. D., Jaslowitz, B., and Craver, L. F. Lymphosarcoma; review of 1296 cases. *Medicine*, 1961, *40*, 31–84.
26. Roulet, F. Das primäre Retothelsarkom der Lymphknoten. *Virchows Arch., path. Anat.*, 1930, *277*, 15–47.
27. Smith, D. F., and Klopp, C. T. Value of surgical removal of localized lymphomas. *Surgery*, 1961, *49*, 469–476.
28. Sternberg, C. Über eine eigenartige unter dem Bilde der Pseudoleukämie verlaufende Tuberculose des lymphatischen Apparatus. *Ztschr. F. Heilk.*, 1898, *19*, 21–90.
29. Stout, A. P. Results of treatment of lymphosarcoma. *New York J. Med.*, 1947, *47*, 158–164.
30. Symmers, D. Giant follicular lymphadenopathy with or without splenomegaly. *A.M.A. Arch. Path.*, 1938, *26*, 603–647.
31. Virchow, R. Die krankhaften Geschwülste. Berlin, A. Hirschwald, 1863, 1.
32. Wilks, S. Cases of enlargement of lymphatic glands and spleen (or Hodgkin's disease). *Guy's Hosp. Rep.*, 1865, *11*, 56–67.

ROLE OF CHEMOTHERAPY IN THE MANAGEMENT OF EARLY HODGKIN'S DISEASE

By DAVID A. KARNOFSKY, M.D., DANIEL G. MILLER, M.D., *and* RALPH F. PHILLIPS, M.D.
NEW YORK, NEW YORK

IN THE present report, the role of available anticancer drugs in the treatment of Stage I and II Hodgkin's disease is to be discussed. This was studied by analyzing our experience in Stage I and II Hodgkin's disease cases, because therapeutic principles that can be defined in this form of lymphoma are more or less applicable to the other histologic types, such as lymphosarcoma, reticulum cell sarcoma and giant follicular lymphosarcoma. However, clinically each of the latter types tends to evolve somewhat differently than Hodgkin's disease; therefore, a discussion of the lymphomas as a single diagnostic entity may lead to errors of generalization.

A number of classifications have been used by clinicians[5,11,17] to describe the extent of Hodgkin's disease, but the one employed by Peters[31,32] is most widely accepted. In this system, each patient is classified according to the following stages: Stage I, involvement of a single site or lymphatic region; Stage II, involvement of 2 or 3 proximal lymphatic regions, (a) with no symptoms of generalized disease and (b) with symptoms of generalized disease; and Stage III, involvement of 2 or more distant lymphatic regions.

In order to "stage" the disease when the patient is first seen, a detailed and orderly effort must be made to determine its extent. Fairly reliable methods are available for the examination of various regions of the body and of organ systems for evidence of Hodgkin's disease. These procedures, which have been emphasized by Kaplan,[18] are listed in Table I.

SYMPTOMS

The absence of symptoms in Stage I and II Hodgkin's disease can be interpreted as a favorable sign,[7] whereas such initial symptoms as weight loss, anorexia, fever, itching, and cough suggest that the disease is generalized, and the prognosis is not nearly as good. Nevertheless, some patients in Stage II, with symptoms such as itching and fever, have shown prolonged responses to local radiation therapy as satisfactory as those occurring in the Stage I asymptomatic patients.

PHYSICAL FINDINGS

A careful examination for enlarged lymph nodes, hepatosplenomegaly and skin involvement is important. The location of the lymphadenopathy and its duration prior to diagnosis have prognostic significance. Enlarged lymph nodes, which come and go or have been present for months without the appearance of enlarged lymph nodes in other areas, suggest a favorable outlook. Localization of the disease to regional lymph nodes is a favorable sign, in contrast to Hodgkin's disease which widely involves lymph node bearing areas, skin, pulmonary parenchyma or nonlymphatic tissues.

LABORATORY FINDINGS

A number of laboratory analyses have been used to determine the extent of the Hodgkin's disease. The blood picture should be studied carefully; anemia, leukocytosis, leukopenia or thrombocytopenia suggest generalized disease. The electro-

---

From the Departments of Medicine and Radiotherapy, Memorial and James Ewing Hospitals and the Division of Clinical Chemotherapy, Sloan-Kettering Institute, New York, New York.

Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1-4, 1963. Part of the Symposium: Lymphomas; Chairman, Dr. James J. Nickson, New York, New York.

This work was supported in part by Research Grant CY-3215 and Program Project Grant 61-77-C-5826 from the National Cancer Institute, Public Health Service.

phoretic pattern may be abnormal, and this may be related to the varied, but sometimes marked impairment of immunologic responsiveness present in Hodgkin's disease.[30] In a number of clinics bone marrow aspirations are obtained, but they have not been highly informative in demonstrating dissemination of Hodgkin's disease.[27] Ley *et al.*[26] at Memorial Hosipital in New York, have been performing Silverman needle biopsies of the posterior iliac crest. This technique seems more likely to reveal bone marrow involvement in lymphomas, particularly in the lymphosarcoma group. Figure 1*A* shows the Silverman needle used and Figures 1, *B*, *C* and *D* show successive enlargements of microscopic views of a specimen of bone marrow obtained from a patient who appeared to have Stage II Hodgkin's disease. The marked fibrosis and the occurrence of suggestive Reed-Sternberg cells are noted and the patient was therefore classified as Stage III. Biochemical measurements of the functional status of major organs, such as the liver and kidneys, should also be recorded.

Table I

PROCEDURES RECOMMENDED FOR THE EVALUATION OF THE EXTENT AND ORGAN INVOLVEMENT OF APPARENTLY LOCALIZED HODGKIN'S DISEASE

Symptoms:	Fever, night sweats
	Weight loss
	Itching
	Weakness
	Cough
Physical Findings:	Lymph Nodes
	Liver
	Spleen
	Skin
Laboratory Findings:	Complete blood cell count, serum electrophoresis
	Kidney and liver function tests
	Bone marrow biopsy
	Roentgen examinations:
	Chest, posteroanterior and lateral
	Abdomen
	Intravenous pyelography
	Inferior vena cavagraphy
	Lymphangiography
	Skeletal survey

Adequate roentgen examinations include chest roentgenograms, a skeletal survey, abdominal roentgenograms, intravenous pyelography, inferior vena cavagraphy and lymphangiography of the inguinal, pelvic and abdominal lymph nodes. While some of these studies may seem unnecessary in presumably Stages I or II cases, they can be revealing, and, in any event, they provide a base-line against which subsequent clinical developments can be evaluated. Lymphangiography, which is now under intensive investigation, may prove to be particularly useful. Lee, Nelson and Schwarz[25] examined by lymphangiography 18 patients with apparently Stage I and II disease, clinically confined to the upper trunk, and 9 were found to have abnormal inguinal, pelvic or abdominal lymph nodes (Fig. 2, *A*, *B* and *C*). A similar proportion of clinically unsuspected involvement in the abdominal lymph nodes (3 of 7 patients) was also found in other types of localized lymphomas. Marchal *et al.*[29] reported that 23 of 45 cases of Hodgkin's disease showed unsuspected enlarged abdominal lymph nodes by lymphangiography. These data suggest that by the routine use of lymphangiography in Stage I and II cases of Hodgkin's disease, perhaps 50 per cent of the patients will show evidence of retroperitoneal involvement.

This clinical evaluation provides for each patient an appreciation of the chronologic evolution, the extent of spread and the organ involvement by Hodgkin's disease. Classifying the lesion into Stage I, II or III[31,32] is a practical step in estimating prognosis and in planning management. The "Stage" classification, however, does not necessarily lead to a clearer understanding of the disease. It suggests that Hodgkin's disease arises as a unifocal process and then progresses, unless treated in some orderly manner, from Stage I to II to III. This is not necessarily true. Some patients with localized Hodgkin's disease may show progressive extension and infiltration into the surrounding tissues over many years without evidence of dissemination, whereas, at the other extreme, Hodgkin's disease is found to be disseminated at the clinical onset, and there is no detectable Stage I or unifocal phase. By describing the varied patterns in the biologic evolution of the disease, we may be able to identify the patients suitable for specific therapeutic measures on a more logical basis than "Stage." For example, a Stage III patient with involvement of pelvic, abdominal, mediastinal and cervical lymph nodes but without symptoms or evidence of organ or bone marrow involvement may be as good a candidate for intensive regional radiation therapy to the involved areas as a Stage I patient with cervical lymphadenopathy. We have nothing better than staging to suggest, however, as a practical means of deciding on treatment, but we believe that a more meaningful classification will be developed which will recognize the histologic characteristics of the involved lymph nodes and the inherent pattern in the clinical onset, location and evolution of the disease.

ROLE OF CHEMOTHERAPY

After the lesion has been classified as Stage I or II, the problem today is to determine the most effective method of controlling or eliminating the disease. Nitrogen mustard is the chemotherapeutic agent most frequently used in the treatment of Hodgkin's disease, but it is indicated principally in Stage III cases. When it has been used as the initial treatment in Stage I, prolonged remissions have sometimes occurred; this is not the usual response and

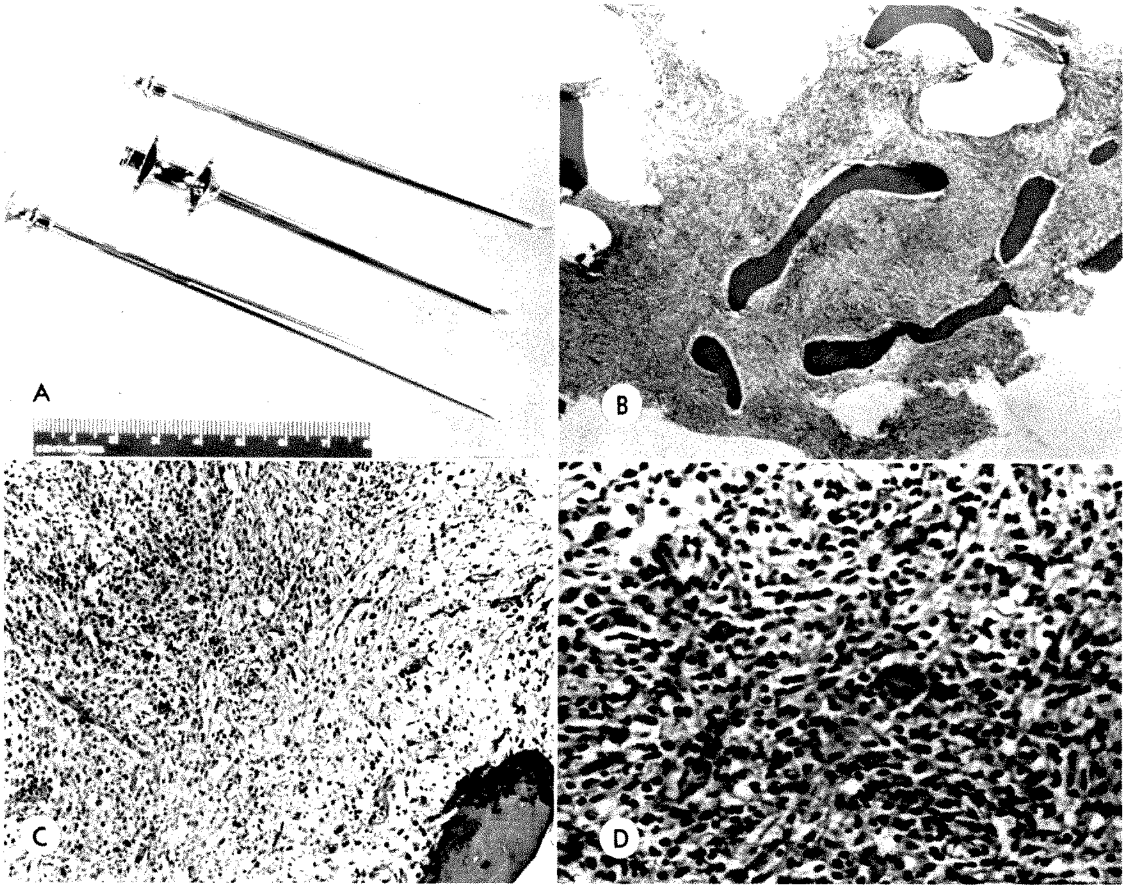


FIG. 1. (*A*) Modified Silverman needle. (*B*) Low-power microscopic view of the bone marrow biopsy section. (*C*) High-power view. (*D*) High-power view showing fibrosis and questionable Reed-Sternberg cells.

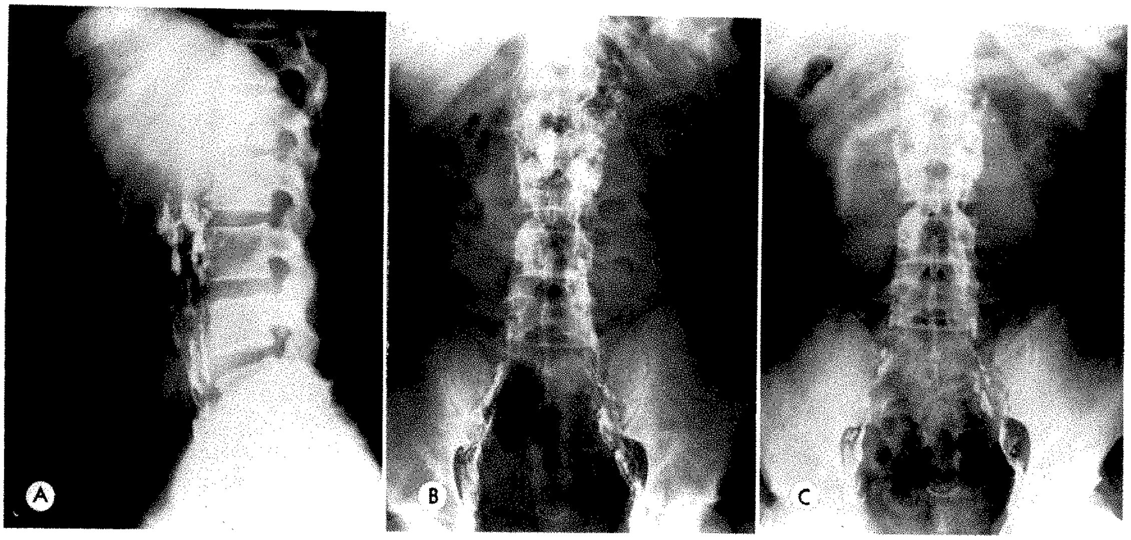


Fig. 2. (*A*) Lateral roentgenogram taken 24 hours after the intralymphatic injection of ethiodol. The contrast medium is concentrated in the lymph nodes and demonstrates abnormal lymph nodes at the level of L2–3. (*B*) Anteroposterior roentgenogram taken 1–2 hours after intralymphatic injection of ethiodol. The lymphatic vessels of the iliac and para-aortic chains are visible with beginning concentration of the contrast material in lymph nodes. Abnormal vessels and lymph nodes are seen at L2–3. (*C*) Anteroposterior roentgenogram in the lymph node phase of case shown in *A* and *B*. Abnormal appearance of lymph nodes at L2 and L3 is apparent.

a prolonged response suggests a relatively slowly progressive process. The average period of improvement after a course of nitrogen mustard is 6 to 10 weeks, and then additional treatment is necessary. Improvement may be maintained for longer periods by the use of oral chlorambucil (leukeran), a congener of nitrogen mustard. It is the consensus, however, that nitrogen mustard does not have a prolonged or profound effect on the course of early Hodgkin's disease,[6,10,12,13,39] and other available anticancer drugs appear to be even less consistently effective.

There is no question that the most effective treatment for localized Hodgkin's disease is radiation therapy. In Stages I and II intensive radiation therapy is directed to the tumor bearing area, and there is accumulating evidence that adjacent lymph node-bearing areas should be irradiated prophylactically.[3,9,14,18,31,32,33,40] This form of treatment may be associated with prolonged control or cure of the disease, and there seems to be no advantage in radical surgery in Stage I Hodgkin's disease.[24,34] It seems likely that the management of regionally localized Hodgkin's disease will become as standardized as radical mastectomy in primary operable breast cancer, and perhaps on better clinical evidence.

What contribution can the available chemotherapeutic agents make to the radiologic management in preventing recurrences and increasing the percentage of patients with possible cure? The correct answer may be that our drugs can add nothing. This abrupt conclusion would be unfair to the serious therapeutic efforts of the chemotherapists in Hodgkin's disease cases. Some of the theoretic and practical reasons for using one chemotherapeutic agent, nitrogen mustard, in Stages I and II of Hodgkin's disease merit discussion.

1. Nitrogen mustard may add to the local antitumor effects of radiation. The mechanism of action of nitrogen mustard in causing regression of enlarged lymph nodes and symptomatic relief in Hodgkin's disease is not known. It may be acting on the neoplastic cells directly by damaging or destroying them, possibly due to its known

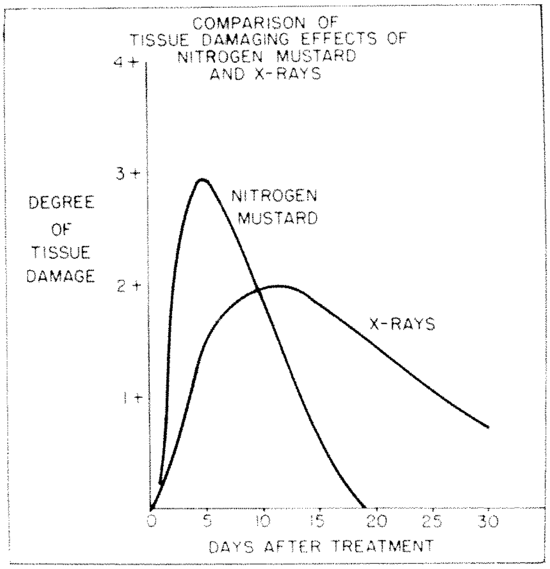


Fig. 3. A diagrammatic comparison of the tissue-damaging effects of clinically tolerated doses of nitrogen mustard and total body irradiation. The plus signs are arbitrary representations of tissue injury and refer to no particular tissue or biologic system.[19]

effect on deoxyribonucleic acid (DNA) or it may be interfering with host reactions to the neoplastic process, of an immune, defensive or induced nature. It has been estimated that the usual course of nitrogen mustard in man, 0.4 mg./kg. of body weight intravenously, produces changes in the bone marrow and peripheral blood picture equivalent to about 150 to 200 r of total body irradiation, and this results in a brief (6 to 10 weeks) and often incomplete response. In some cases, while nitrogen mustard produces symptomatic relief, lymph node enlargement may continue. Furthermore, at equivalent degrees of toxicity, as measured by toxicity in laboratory animals or by depression of the blood picture in man, the onset of toxicity and recovery from nitrogen mustard is more rapid than after equivalent doses of total body irradiation. This is shown diagrammatically in Figure 3.[19] Recently, Kretchmar *et al.*[23] have made a similar observation, and stated, "It is of interest that the bone marrow depression developed and recovery began earlier (in their clinical study with nitrogen mustard) than after a dose of total-body irradiation that produced comparable damage to the hematopoietic system." There is evidence that nitrogen mustard may have an additive or greater than additive effect when used in combination with total body irradiation in mice. In one study nitrogen mustard given before total body irradiation was more than additive, whereas, in the reverse sequence, toxicity was decreased.[20] For this reason when nitrogen mustard was combined with radiation therapy, the drug was given just prior to local irradiation.[21] This sequence did not seem to aggravate the systemic bone marrow depression produced by either agent and recovery of the peripheral blood count from the nitrogen mustard proceeded while irradiation was continued to the local area. It is, therefore, possible that nitrogen mustard given in combination with radiation therapy may appreciably enhance the local therapeutic effect of radiation, perhaps to a greater extent than the estimated 150 r to 200 r equivalent of nitrogen mustard. Since large doses of roentgen rays, with or without nitrogen mustard, can obliterate the local disease, it is uncertain if nitrogen mustard can make a significant contribution to the long-term result. Nevertheless, it is not known whether roentgen rays act by destroying all the neoplastic cells, or possibly by altering the local tissues so that they are no longer capable of supporting the cell types involved in Hodgkin's disease. Sykes *et al.*[36] have shown that, when the bone marrow is irradiated locally in man with tissue doses in the range of 3,400 rads or more, the marrow does not recover in this area, whereas recovery occurs at lower doses in the range of 2,000 rads. The failure to recover at the high doses is possibly due to alterations in the bone marrow environment, so that hematopoietic cells no longer have a proper environment for growth and differentiation. If this proposed mechanism is operative in regard to the growth of Hodgkin's disease in lymph nodes, perhaps nitrogen mustard may contribute to this indirect action of radiation in preventing local recurrence.

2. Nitrogen mustard may act on clinically undetectable areas of involvement outside of the irradiated area. The use of nitrogen mustard as adjuvant chemotherapy in Hodgkin's disease was proposed by several workers.[3,6] There are no statistical studies, however, that a course of nitrogen mustard, or of any of the other alkylating agents, prevents or delays the recurrence of Hodgkin's disease, but it is a matter that requires further study.[4] There is no doubt that by the use of maintenance therapy with the alkylating agents, recurrence would be delayed in some cases, but this would not necessarily mean that life was prolonged.

3. Pretreatment with nitrogen mustard may produce prompt relief of symptoms and prevent local edema which is sometimes reported to follow the initiation of radiation therapy. A course of nitrogen mustard immediately prior to radiation therapy appears to be a useful procedure in treating such problems as a superior vena cava compression syndrome, massive disease in the cervical region or impending cord compression.

4. Pretreatment with nitrogen mustard may encourage aggressive radiation therapy. This may appear to be a specious argument, but, in setting up an experimental program of aggressive local and prophylactic radiation therapy, the use of nitrogen mustard as part of the study appeared to diminish certain reservations the radiotherapist had concerning the administration of rapid and intensive irradiation. Today, with a great deal of experience with intensive large-field radiation therapy[18] nitrogen mustard need no longer bear the onus of an experimental program.

5. Hodgkin's disease presents varied and interesting biochemical, hematologic and immunologic disturbances. The internist usually administers the nitrogen mustard and thus participates in the management and follow-up of the patient. Chemotherapy has given him a wedge whereby he can become actively involved in the care of patients in the early, as well as in the advanced, stages of the disease. This early participation by the internist can only be of benefit to the patient.

DISCUSSION

For the reasons noted, we began in 1949 to treat Stage I or II patients with involvement of the thorax or neck with 0.4 mg./kg. of nitrogen mustard intravenously followed by irradiation to the local disease and regional lymph nodes. In most cases, 3,000 rads were given to the cervical, mediastinal and axillary lymph nodes *en bloc* in 8 to 10 days.[21] While it was planned to deliver 3,000 rads to the entire volume of tissue, this dose was not always reached, but in no case was the tissue dose less than 2,500 rads. It was not an organized program, and Stage I and II patients were treated if directly referred to one of us. Patients in the advanced stages of Hodgkin's disease are generally sent to chemotherapists and only 22 cases could be placed in this series.

Figure 4 shows the results in 22 cases treated by this method. Other than the sore throat and esophagitis following radiation therapy, complications have been negligible. Of 13 patients now apparently free of disease since their initial therapy, 8 have survived longer than 5 years. Of 4 patients alive with recurrent disease, 3 had recurrences in an unirradiated axilla and 1 in the inguinal area. Possibly the 3 with recurrent disease would have remained free of disease if the axillae had been irradiated initially. While there were no recurrences in the irradiated areas, 5 patients in this series have died of their disease with intra-abdominal or inguinal lymph node recurrences from disease initially treated in the upper trunk. Thus, of 17 patients, 8 or 47 per cent are alive and have remained apparently free of disease for 5 years or more, 4 (24 per cent) are alive having had recurrent

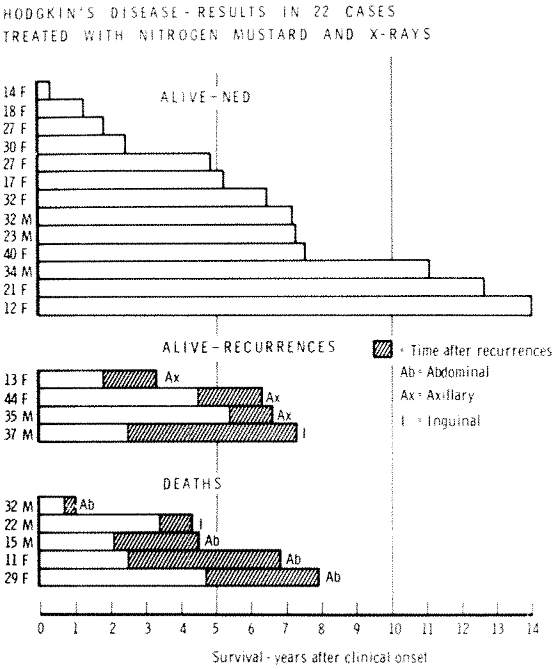


Fig. 4. Course of Stage I and II Hodgkin's disease in 22 patients treated with a combination of nitrogen mustard and intensive regional radiation therapy. At the left the age of onset and the sex of the patients are given. NED—no evidence of disease, ☐—no evidence of recurrent disease.

disease, but 3 have lived longer than 5 years thus far, and 5 (29 per cent) are dead. Eleven of 16 patients (70 per cent) are alive 5 years or longer and 5 patients (30 per cent) have died.

We do not know if nitrogen mustard contributed anything to these results, but it did not appear to cause obvious adverse effects. Linke[28] reported remarkable additional benefit from radiation therapy when given in combination with an alkylating agent, *p*-benzoquinone,2,3, 5-tris (1-aziridinyl)-trenimon, a soluble form of E-39 (Fig. 5). There was definite improvement in the 5 year survival figures at all stages, but when he compared his results with those of Peters, who used roentgen therapy alone, the additional benefit from trenimon was not apparent. He did not describe the dosage used in his study, and possibly the alkylating agent compensated for less aggressive irradiation.

While we have employed intravenous nitrogen mustard in our studies, other drugs also have a useful effect on advanced Hodgkin's disease. In Figure 6 are shown some alkylating agents of current interest. Possibly one of these agents, given as an intensive course of treatment, or prophylactically, by intermittent administration after the completion of radiation therapy may be more useful than nitrogen mustard in prolonging control of the disease. Actinomycin C and D[1,37] also have some effect on Hodgkin's disease, and actinomycin D has been shown to exacerbate the skin reactions when it is given after radiation therapy. This suggests the possibility that it may also potentiate the effect of radiation on Hodgkin's disease. Vincristine and vinblastine (Velban, VLB) are being used in disseminated Hodgkin's disease and have a beneficial effect in some cases.[2,15,16,38] Their capability to enhance the effects of roentgen

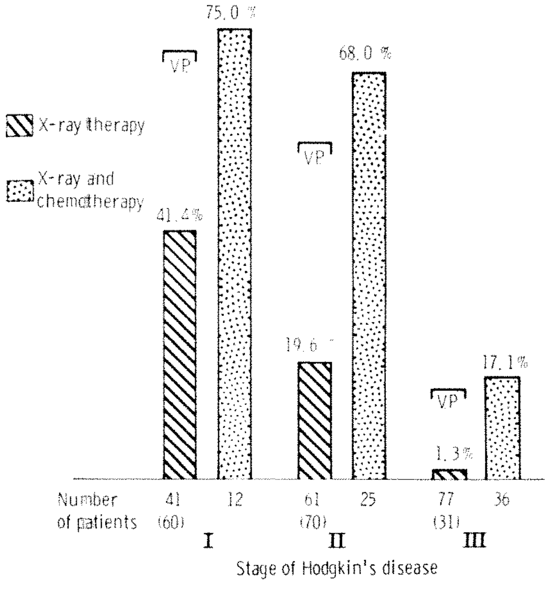


Fig. 5. Adapted from Linke.[28] Five year survival of 252 patients with Hodgkin's disease classified by Stage of disease and treated by radiation therapy alone or in combination with an alkylating agent (trenimon—2,3,5-tris-ethyleneiminobenzoquinone, 1,4, a soluble form of E-39). V.P. refers to results obtained by Peters in patients treated by roentgen therapy alone at the same stages of Hodgkin's disease. The numbers of cases in parentheses at the bottom of the figure refer to Peters' cases.

rays has not been demonstrated, and requires study. The adrenal cortical hormones are also occasionally helpful in advanced stages of Hodgkin's disease.[22]

Stein[35] and Fletcher *et al.*[8] have indicated the difficulties in evaluating a therapeutic combination of irradiation and chemotherapy, particularly when the drug by itself occasionally has an independent effect on the disease. It is very difficult to determine whether chemotherapy adds to or potentiates the effects of radiation on neoplastic tissues, and the possibility that drugs may interfere with the effects of radiation must also be considered.

SUMMARY

1. The necessary diagnostic procedures in relation to the "staging" of Hodgkin's disease and a policy for treating Stage I and II with high doses of roentgen rays to the tumor-bearing and adjacent lymph node areas have been discussed.

2. There appears to be no indication for the use of any available chemotherapeutic agent alone in the treatment of Stage I and II Hodgkin's disease. Conclusive evidence has not been developed that the combination of an alkylating agent and local radiation therapy gives therapeutic results superior to those with radiation therapy alone. However, some theoretic and practical justifications for combining these agents have been listed.

3. Chemical variants of the polyfunctional alkylating agents and other types of anticancer drugs, such as actinomycin D, vinblastine, vincristine and prednisone, have measurable therapeutic effects on Hodgkin's disease. Their value in Stage I or II alone or in combination with local radiation therapy has not been evaluated.

4. It is recommended that interinstitutional cooperative protocol studies be organized to determine the value of these drugs in combination with carefully programmed irradiation so as to achieve complete control of the local disease in Stage I and II and to delay recurrences in generalized disease.

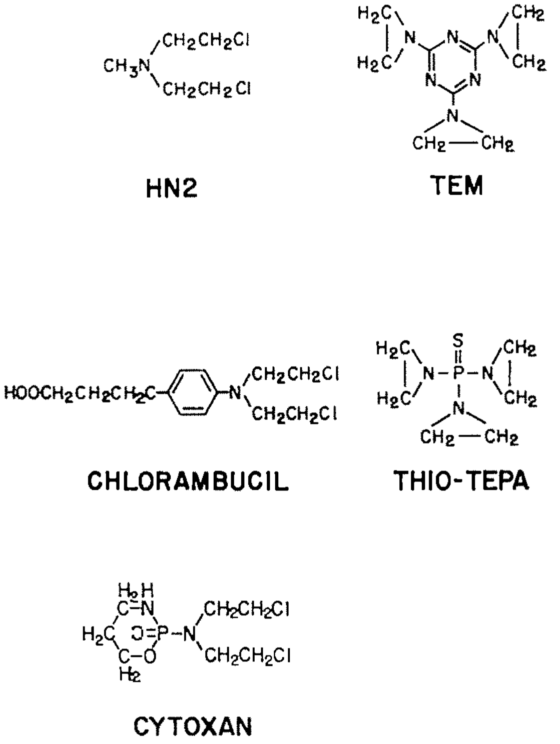


Fig. 6. Formulae of polyfunctional alkylating agents related to nitrogen mustard and used in the treatment of Hodgkin's disease.

5. It is no longer appropriate to treat Stage I and II Hodgkin's disease with unplanned, episodic and trivial radiologic attacks on the most apparent manifestations of the disease or with chemotherapeutic agents alone. Of all cases with Hodgkin's disease, 20 to 40 per cent are in true Stage I or II at the time of diagnosis, and thus have a good chance of obtaining prolonged control and possibily cure from adequate radiation therapy. The simultaneous use of chemotherapy, such as nitrogen mustard, may possibly improve the results. It would be desirable, where optimal diagnostic and therapeutic facilities are not available, to refer the patient to designated, cooperating institutions where effective treatment can be given and reliable information obtained in statistically oriented studies.

David A. Karnofsky, M.D.
Memorial Hospital for Cancer and Allied Diseases
444 East 68th Street
New York 21, New York

We wish to thank Miss Meta E. Buehler, R.N., for her assistance in the review of patient records.

REFERENCES

1. Begemann, H. Clinical experience with actinomycin C. *Ann. New York Acad. Sc.*, 1960, *89*, 454–462.
2. Bohannon, R. A., Miller, D. G., and Diamond, H. D. Vincristine in treatment of lymphomas and leukemias. *Cancer Res.*, 1963, *23*, 613–621.
3. Brown, F. A., and Kaplan, H. S. Hodgkin's disease: revised clinical classification and approach to treatment of its localized form. *Stanford M. Bull.*, 1957, *15*, 183–190.
4. Cook, J. C., Krabbenhoft, K. L., and Leucutia, T. Combined radiation and nitrogen mustard therapy in Hodgkin's disease as compared with radiation therapy alone. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *82*, 651–657.
5. Craver, L. F. Some aspects of treatment of Hodgkin's disease. *Cancer*, 1954, *7*, 927–933.
6. Dameshek, W., Weisfuse, L., and Stein, T. Nitrogen mustard therapy in Hodgkin's disease; analysis of fifty consecutive cases. *Blood*, 1949, *4*, 338–379.
7. Finkbeiner, J. A., Craver, L. F., and Diamond, H. D. Prognostic signs in Hodgkin's disease. *J.A.M.A.*, 1954, *156*, 472–477.
8. Fletcher, G. H., Suit, H. D., Howe, C. D., Samuels, M., Jesse, R. H., Jr., and Villareal, R. U. Clinical method of testing radiation-sensitizing agents in squamous cell carcinoma. *Cancer*, 1963, *16*, 355–363.
9. Fuller, L. M., and Fletcher, G. H. Radiotherapeutic management of lymphomatous diseases. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *88*, 909–923.
10. Gellhorn, A., and Collins, V. P. Quantitative evaluation of contribution of nitrogen mustard to therapeutic management of Hodgkin's disease. *Ann. Int. Med.*, 1951, *35*, 1250–1259.
11. Gilbert, R. Radiotherapy in Hodgkin's disease (malignant granulomatosis); anatomic and clinical foundations; governing principles; results. Am. J. Roentgenol. & Rad. Therapy, 1939, *41*, 198–241.
12. Hall, C. A., and Olson, K. B. Therapy of malignant lymphomas. I. Study of 116 cases. *Am. J. Med.*, 1956, *20*, 392–398.
13. Hall, C. A., and Olson, K. B. Therapy of malignant lymphomas. II. Review. *Am. J. Med.*, 1956, *20*, 399–411.
14. Healy, R. J., Amory, H. I., and Friedman, M. Hodgkin's disease; review of two hundred and sixteen cases. *Radiology*, 1955, *64*, 51–55.
15. Hill, J. M., and Loeb, E. Treatment of leukemia, lymphoma, and other malignant neoplasms with vinblastine. *Cancer Chemotherapy Reports*, 1961, *15*, 41–61.
16. Hodes, M. E., Rohn, R. J., and Bond, W. H. Vincaleukoblastine. I. Preliminary clinical studies. *Cancer Res.*, 1960, *20*, 1041–1049.
17. Jelliffe, A. M., and Thomson, A. D. Prognosis in Hodgkin's disease. *Brit. J. Cancer*, 1955, *9*, 21–36.
18. Kaplan, H. S. Radical radiotherapy of regionally localized Hodgkin's disease. *Radiology*, 1962, *78*, 553–561.
19. Karnofsky, D. A., and Burchenal, J. H. Present status of clinical cancer chemotherapy. *Am. J. Med.*, 1950, *8*, 767–788.
20. Karnofsky, D. A., Burchenal, J. H., Ormsbee, R. A., Cornman, I., and Rhoads, C. P. Experimental observations on use of nitrogen mustards in treatment of neoplastic disease. Approaches to Tumor Chemotherapy AAAS, 1947, 293–305.
21. Karnofsky, D. A., Myers, W. P. L., and Phillips, R. Treatment of inoperable pulmonary cancer, primary and metastatic. *Am. J. Surg.*, 1955, *89*, 526–537.
22. Kofman, S., Perlia, C. P., Boesen, E., Eisenstein, R., and Taylor, S. G. III. Role of corticosteroids in treatment of malignant lymphomas. *Cancer*, 1962, *15*, 338–345.
23. Kretchmar, A. L., Andrews, G. A., and Sitterson, B. W. Attempts at bone-marrow autografts after large doses of nitrogen mustard. *New England J. Med.*, 1963, *268*, 427–428
24. Lacher, M. J. Role of surgery in Hodgkin's disease. *New England J. Med.*, 1963, *268*, 289–292.
25. Lee, B., Nelson, J., and Schwarz, G. Personal communication, 1963.
26. Ley, A. B., Prendergast, R. A., and Hartmann, W. H. Silverman needle biopsy of bone marrow. *M. Clin. North America*, 1961, *45*, 553–561.
27. Limarzi, L. R., and Paul, J. T. Sternal marrow studies in Hodgkin's disease; review of literature and report of thirty-five cases. *Am. J. Clin. Path.*, 1949, *19*, 929–961.
28. Linke, A. Die Behandlung der Hämoblastosen und malignen Tumoren mit Trisaethyleniminobenzochinon. *Deutsch. Med. Wchnschr.*, 1960, *85*, 1928–1933.
29. Marchal, G., Bernard, J., Arvay, N., Bilski-Pasquier, G., Picard, J. D., Mathe, G., and Brule, G. La lymphographie dans la maladie de Hodgkin (étude de 45 cas). *Nouv. Rev. franç. Hémat.*, 1962, *2*, 4–26.
30. Miller, D. G. Patterns of immunological deficiency in lymphomas and leukemias. *Ann. Int. Med.*, 1962, *57*, 703–716.
31. Peter , M. V. Study of survivals in Hodgkin's

disease treated radiologically. Am. J. Roentgenol. & Rad. Therapy, 1950, *63*, 299–311.

32. Peters, M. V., and Middlemiss, K. C. H. Study of Hodgkin's disease treated by irradiation. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1958, *79*, 114–121.
33. Roos, D., and Videbaek, A. Prognosis in Hodgkin's disease. *Danish Med. Bull.*, 1959, *6*, 177–181.
34. Slaughter, D. P., and Craver, L. F. Hodgkin's disease; five year survival rate; value of early surgical treatment; notes on four cases of long duration. Am. J. Roentgenol. & Rad. Therapy, 1942, *47*, 596–606.
35. Stein, J. J. Question of chemical potentiators in radiation therapy. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *88*, 989–992,
36. Sykes, M. P., Chu, F. C. H., and Wilkerson, W. G. Local bone-marrow changes secondary to therapeutic irradiation. *Radiology*, 1960, *75*, 919–924.
37. Tan, C. T., Golbey, R. B., Yap, C. L., Wollner, N., Hackethal, C. A., Murphy, L. M., Dargeon, H. W., and Burchenal, J. H. Clinical experiences with actinomycins D, KS2, and F1 (KS4). *Ann. New York Acad. Sc.*, 1960, *89*, 426–444.
38. Warwick, O. H., Darte, J. M. M., Brown, T. C., Beer, C. T., Cutts, J. H., and Noble, R. L. Some biological effects of vincaleukoblastine, alkaloid in vinca rosea in patients with malignant disease. *Cancer Res.*, 1960, *20*, 1032–1040.
39. Warwick, O. H., and Sellers, A. H. Symposium on Hodgkin's disease based on series of 960 cases diagnosed clinically. *Canadian M. A. J.*, 1959, *80*, 423–429.
40. Zanca, P., Brascho, D. J., and Fagan, C. J. Treatment of Hodgkin's disease; review of 118 cases. *Am. Pract. & Digest Treat.*, 1962, *13*, 399–402.

CERVICAL LYMPH NODE INVOLVEMENT IN ORAL CANCER*

By ROBERT A. MUSTARD, M.D., *and* IRVING B. ROSEN, M.D.
TORONTO, ONTARIO, CANADA

THIS report is based on a study of all 1,177 cases of squamous cell carcinoma of the oral cavity admitted to the Toronto General Hospital during 15 years, 1942–1956 inclusive. It is part of the series reported by Ash in his Janeway Lecture of 1961,[1] and it is an extension of the work reported by Wookey and associates in 1951.[2]

Our objective has been to examine those aspects of the management of oral cancer which are related to the question of involvement of cervical lymph nodes. It must be appreciated that the Oral Cancer Clinic at the Toronto General Hospital has been organized and controlled by the Department of Radiotherapy. Irradiation has, therefore, played a dominant role in the management of these cases; surgeons, including the senior author (R.A.M.), have attended as Consultants. Friendly and effective cooperation has been assured by mutual acceptance of a treatment policy under which primary intraoral lesions are usually managed by radiation therapy, while involved neck lymph nodes, whenever possible, are dealt with by surgical measures, preferably radical neck dissection. With few exceptions, surgical excision of primary oral cancer has been reserved for radiation failures or for the complications of irradiation such as chronic ulceration or bone necrosis. In dealing with the areas of regional lymphatic spread, irradiation has generally been employed only when operation was contraindicated either by the extent of disease or by the condition of the patient.

The effectiveness of this treatment policy is indicated by the 5 year survival rates for the whole group (Table I). Of 1,177 patients with oral cancer, 368 were alive at 5 years from the date of registration—a crude survival rate of 31.3 per cent. Excluding 161 patients who died of extraneous disease and 47 who were untraced, we obtain a net survival rate for determinate cases of 38.1 per cent.

INCIDENCE AND SIGNIFICANCE OF CERVICAL LYMPH NODE INVOLVEMENT

The incidence of cervical lymph node involvement according to the site of primary tumor is shown in Table II. Buccal mucosa lesions have the lowest total incidence of lymph node involvement (38.8 per cent); this correlates well with the highest net survival rate (49.2 per cent) as shown in Table I.

There were 547 patients (46.4 per cent of the total series) who had no apparent involvement of neck lymph nodes at any time; this group had a net 5 year survival rate of 64.2 per cent (Table III). The remaining 630 patients (53.6 per cent of the total series) who had either clinical or pathologic evidence of spread to cervical lymph nodes had a net survival rate at 5 years of 20.4 per cent. When neck lymph nodes were judged to be involved at the time of admission (341 cases or 29.0 per cent of the total series), the net survival rate at 5 years was only 15.0 per cent. In 289 cases (24.6 per cent of the total series) in which enlarged lymph nodes appeared at some later date, the net 5 year survival rate was 27.8 per cent.

RADIATION THERAPY OF INVOLVED NECK LYMPH NODES

In 257 of the 630 patients considered to

---

* Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963. Part of the Symposium: Management and End Results in the Treatment of Metastatic Cervical Lymph Nodes; Chairman, Dr. William S. MacComb, Houston, Texas.

Table I

FIVE YEAR SURVIVAL RATES IN ALL CASES OF ORAL CANCER (1942–1956)

Site	No. of Cases	Total Alive at 5 Years	Survival Rate (%)	
			Crude	Net*
Floor of Mouth	128 (10.9%)	46	35.9	42.6
Tongue	464 (39.4%)	136	29.3	33.7
Gingiva	263 (22.4%)	75	28.5	35.2
Palate	85 (7.2%)	22	25.9	34.4
Buccal Mucosa	237 (20.1%)	89	37.6	49.2
All Cases	1,177 (100%)	368**	31.3	38.1

* Untraced cases and those known to have died of extraneous disease are excluded.
** Includes 28 alive with disease.

have involved neck lymph nodes, the sole treatment to the neck was some form of irradiation. The net 5 year survival rate in this group was 11.7 per cent (Table iv).

It must be emphasized that these were mostly unfavorable cases in which surgical treatment of lymph nodes was contraindicated because either the primary lesion or its cervical secondaries appeared incurable or inoperable. However, it should also be noted that in none of the 22 five year survivors free of disease was there pathologic confirmation that the lymph nodes were actually involved by carcinoma.

SURGICAL TREATMENT OF NECK LYMPH NODES

Of the 1,177 cases studied, surgical treatment to cervical lymph node areas was undertaken in 291 (25 per cent). Fourteen of these died of extraneous disease and 1 was untraced, leaving as a determinate group 276 patients of whom 89 were living at 5 years from registration; *i.e.*, a net survival rate of 32.2 per cent (Table v). Sixty-eight (76 per cent) of these long survivors had pathologically positive lymph nodes.

It should be noted that under our treatment policy neck dissection has been done only when apparently involved lymph nodes were detected, not infrequently several years after the date of registration. Allowance for this is made in Table v by calculating survival from the date of the last major neck operation. Seventy-three of 276 patients were living 5 years after operation, giving a net postoperative survival rate of 26.4 per cent.

The operative procedure in 242 cases (Table vi) involved the neck only—unilateral or bilateral radical neck dissection 194 cases, upper neck dissection 35 cases, and local excision of lymph nodes 13 cases. In most of these, the indication for operation was enlarged excepting the operable cervical lymph nodes in the presence of a primary tumor, either controlled or considered likely to be controlled by radiation therapy. In 223 (91.8 per cent) the removed lymph nodes were noted to contain metastatic carcinoma. The net 5 year survival rate from the time of admission was 31.6 per cent, from the date of the last neck operation 26.4 per cent.

Combined operation on the primary tumor plus neck dissection was performed in 48 cases (Table vii). In 10 of these the operation was planned primarily to deal with lymph nodes, the mouth lesion being separately excised because its control was doubtful. In the other 38 cases the main objective of the surgical procedure was to deal with residual or recurrent primary disease—neck dissection in continuity was a logical extension. The lymph nodes removed in these 48 cases were pathologically positive in 34 instances (70.8 per cent). The net 5

Table II

LYMPH NODE INVOLVEMENT BY SITE IN ALL CASES OF ORAL CANCER (1942–1956)

Time of Lymph Node Involvement	Floor of Mouth	Tongue	Gingiva	Palate	Buccal Mucosa	All Cases
No Involved Lymph Nodes at Any Time	52 (39.8%)	176 (37.9%)	131 (50.0%)	44 (52.0%)	145 (61.2%)	547 (46.4%)
Lymph Nodes Involved on Admission	43 (33.6%)	141 (30.4%)	82 (31.1%)	21 (24.7%)	54 (22.8%)	341 (29.0%)
Lymph Nodes Involved Later	34 (26.6%)	147 (31.7%)	50 (18.9%)	20 (23.3%)	38 (16.0%)	289 (24.6%)
All Cases with Lymph Node Involvement	77 (60.2%)	288 (62.1%)	132 (50.0%)	41 (48.0%)	92 (38.8%)	630 (53.6%)
All Cases	128 (100%)	464 (100%)	263 (100%)	85 (100%)	237 (100%)	1,177 (100%)

year survival rates were from the date of admission 36.4 per cent and from the last operation 27.3 per cent.

CAUSES OF FAILURE IN CASES RECEIVING SURGICAL TREATMENT TO NECK LYMPH NODES

Postoperative deaths accounted for 16* (5.5 per cent) of the 291 surgically treated patients. For combined operations the rate was 5 of 48 patients, *i.e.*, 10.4 per cent. From 243 operations involving the neck only, there were 11 deaths, *i.e.*, 4.5 per cent.

We have attempted to ascertain the status at death of all 190 patients having surgical treatment to the neck lymph nodes who died of their malignant disease at any time up to 10 years from registration (Table viii). In 20 cases distant metastases were observed. In 46 cases (24 per cent of those who died of disease), uncontrolled

---

* Only 1 of these deaths occurred during the last 5 years studied, *i.e.*, 1952–1956 inclusive.

Table III

NET 5 YEAR SURVIVAL RATES BY LYMPH NODE INVOLVEMENT IN ALL CASES OF ORAL CANCER (1942–1956)

Time of Lymph Node Involvement	Floor of Mouth (%)	Tongue (%)	Gingiva (%)	Palate (%)	Buccal Mucosa (%)	All Cases (%)
No Involved Lymph Nodes at Any Time	71.4	62.2	57.7	53.3	72.6	64.2
Lymph Nodes Involved on Admission	23.1	11.9	18.3	11.1	12.8	15.0
Lymph Nodes Involved Later	35.3	27.7	13.6	25.0	40.0	27.8
All Cases with Lymph Node Involvement	28.8	19.9	15.6	17.1	23.3	20.4

Table IV

NET 5 YEAR SURVIVAL RATES IN CASES OF ORAL CANCER WITH INVOLVED LYMPH NODES TREATED ONLY BY IRRADIATION (1942–1956)

Site	No. Treated	No. Alive at 5 Years	Net Survival Rate (%)
Floor of Mouth	39	7	18.4
Tongue	106	6	5.9
Gingiva	56	10	20.4
Palate	18	2	12.5
Buccal Mucosa	38	3	8.8
All Cases	257	28*	11.7

* Includes 6 cases alive with disease.

disease of the neck lymph nodes was the only apparent finding at death.

Recurrence at the primary site was responsible for failure of treatment in 117 cases—62 per cent of all disease mortality. About half of these also had further lymph node involvement, in most instances clearly attributable to the reactivated primary neoplasm.

It should be noted that even among those who had operation on the neck only (their primary tumor being "controlled" by irradiation) regrowth of the primary lesion was recorded at death in 91 cases while further lymph node involvement as the only manifestation of disease was seen in only 45 cases.

Recurrence of the primary tumor has been the most common cause of failure in cases receiving surgical treatment to the neck lymph nodes. The apparent control of the intraoral lesion by irradiation is often merely temporary arrest—neck dissection during this quiescent period is frequently followed, sometimes after a surprisingly long interval, by recurrent growth in the mouth.

The appearance of cervical metastases may thus be considered to have an ominous significance in regard to the nature of the primary tumor. It suggests a dangerously aggressive disease which in many instances is merely restrained, not obliterated, by irradiation alone. It would seem logical to excise such lesions before the dormant tumor regains its vigor. Therefore, it is proposed that, as a general rule, whenever neck dissection is undertaken, the primary site should at the same time be widely removed even though the disease there appears controlled by radiation therapy.

FACTORS AFFECTING SURVIVAL AFTER SURGICAL TREATMENT OF NECK LYMPH NODES

The factors listed below might reasonably be expected to influence the survival rate after the surgical treatment of neck lymph nodes. It must, however, be emphasized that their full significance is almost

Table V

NET 5 YEAR SURVIVAL RATES IN CASES OF ORAL CANCER WITH INVOLVED LYMPH NODES TREATED SURGICALLY (1942–1956)

Site	No. Treated	No. Living at 5 Years from Registration	Net Survival Rate (%)	No. Living at 5 Years from Last Operation	Net Postoperative Survival Rate (%)
Floor of Mouth	32	14	46.7	12	40.0
Tongue	147	45	32.4	34	24.5
Gingiva	49	9	19.6	9	19.6
Palate	18	5	29.4	5	29.4
Buccal Mucosa	45	16	36.4	13	29.6
All Cases	291	89*	32.2	73	26.4

* Includes 4 cases alive with disease.

TABLE VI

NET 5 YEAR SURVIVAL RATES IN CASES OF ORAL CANCER WITH INVOLVED LYMPH NODES TREATED BY OPERATION TO NECK ONLY (1942–1956)

Operative Procedure	No. Treated	No. Living at 5 Years from Registration	Net Survival Rate (%)	No. Living at 5 Years from Last Operation	Net Postoperative Survival Rate (%)
Local excision only	13	6	50.0	4	33.3
Unilateral radical neck dissection	184	55	31.6	47	26.9
Radical dissection on one side plus upper neck dissection on other side	4	1	†	—	—
Simultaneous bilateral radical neck dissection	6	2	†	2	†
Unilateral upper neck dissection	29	7	25.0	6	21.4
Bilateral upper neck dissection	6	2	†	2	†
All Cases	242*	73	31.6	61	26.4

* Excludes 1 case with type of operation not stated.
† Rates not calculated for less than 10 cases.

certainly obscured by the over-riding effect of the criteria governing selection of patients in this series for operation; namely, (a) apparent resolution of primary tumor following initial radiation therapy, (b) cervical lymph nodes enlarged but operable, and (c) no evidence of metastatic spread.

1. *Site of Primary Tumor* (*Table* v). Our best results have been obtained with the small group (32 cases) in which the primary lesion was in the floor of the mouth. Fol-

TABLE VII

NET 5 YEAR SURVIVAL RATES IN CASES OF ORAL CANCER TREATED BY COMBINED EXCISION OF PRIMARY LESION AND LYMPH NODE AREAS (1942–1956)

Operative Procedure	No. Treated	No. Living at 5 Years from Registration	Net Survival Rate (%)	No. Living at 5 Years from Last Operation	Net Postoperative Survival Rate (%)
Excision of primary tumor plus separate radical neck dissection	10	5	†	4	†
Excision of primary tumor plus in continuity upper neck dissection	16	3	21.4	1	7.1
Excision of primary tumor plus in continuity radical neck dissection	22	8	38.1	7	33.3
All Cases	48*	16	36.4	12	27.3

* Floor of mouth—5 cases; tongue—19 cases; gingiva—13 cases; buccal mucosa—11 cases.
† Rates not calculated for less than 10 cases.

Table VIII

CAUSES OF FAILURE IN CASES OF ORAL CANCER RECEIVING SURGICAL TREATMENT TO NECK LYMPH NODES (1942–1956)

Operative Procedure	Total Deaths from Disease up to 10 Years from Admission	Status at Death				
		Primary Lesion Uncontrolled	Primary Lesion and Lymph Nodes Uncontrolled	Lymph Nodes Uncontrolled	Metastases Uncontrolled	Not Stated
Operation on neck lymph nodes only	163	46	45	45	20	7
Combined excision of primary tumor plus lymph node area	27	11	15	1	—	—
Total	190	57	60	46	20	7

lowing operation there was a net 5 year survival rate from the time of admission of 46.7 per cent. The poorest group has been the 49 patients with primary gingival lesions; the net 5 year survival rate was 19.6 per cent. Tongue cancer patients formed much the largest group, 147 cases with a net 5 year survival rate of 32.4 per cent. The differences between the rates of survival for tumors arising in different portions of the tongue (Table IX) are less striking than one would have anticipated (*vide supra*).

2. *Staging of Primary Tumor* (*Table* X). We have used the stage classification for oral cavity lesions proposed in 1962 by the American Joint Committee on Cancer Staging and End Results Reporting:

T1—tumor up to 3 cm.
T2—tumor over 3 cm.
T3—tumor involving other structures
T4—tumor with extensive involvement of other structures

It should be noted that Stage T1 includes Stages I and II of the Richards classification as used by Ash in the Janeway Lecture of 1961.

Of the 291 patients under consideration, 168 (57.7 per cent) had primary tumors classified T1 on admission. These had a net 5 year survival rate of 37.4 per cent. Among much smaller groups in the T2, T3 and T4 categories, the equivalent rates were 23.1, 21.6 and 26.3 per cent, respectively.

The best results from neck dissection were obtained in patients who had small primary lesions. The relatively good results in those who on admission had larger primary tumors are probably accounted for by factors of selection as discussed above.

3. *Time of Appearance of Neck Lymph Node Involvement.* We have already seen

Table IX

NET 5 YEAR SURVIVAL OF TONGUE CANCER CASES WITH SURGICAL TREATMENT TO NECK LYMPH NODES (1942–1956)

Subsite	Total No.	Total Alive At 5 Years	Net 5 Year Survival (%)
Anterior two-thirds	83	26	32.9
Posterior one-third (back to glossopalatine fold)	41	14	37.8
Base of tongue	20	4	20.0
Whole tongue	2	1	—*
Whole lateral border	1	—	—
All Cases	147	45	32.4

* Rate not calculated for fewer than 10 cases.

Table X

NET 5 YEAR SURVIVAL RATES BY STAGE OF PRIMARY TUMOR AT ADMISSION IN CASES OF ORAL CANCER RECEIVING SURGICAL TREATMENT TO LYMPH NODES (1942–1956)

Category	Total Cases		Total Alive at 5 Years	Net Survival Rate (%)
	No.	%		
T1	168	57.7	58	37.4
T2	40	13.8	9	23.1
T3	52	17.9	11	21.6
T4	19	6.5	5	26.3
Not stated	12	4.1	6	50.0
All Cases	291	100	89	32.2

(Table III) that for the entire series of 1,177 cases those who had involved neck lymph nodes on admission had a much poorer survival rate than those who were later found to have enlarged lymph nodes.

The same relationship holds true in the subgroup of 291 patients who were selected for surgical treatment to the neck area (Table XI). Those with involved lymph nodes on admission, 119 patients, had a net 5 year survival rate of 17.7 per cent. For 78 patients in whom metastasis to the neck became apparent from 1 to 11 months after registration, the rate was 33.3 per cent. When enlarged lymph nodes were not detected until 1 year or more after admission, the net rate of 5 year survival was 51.1 per cent.

The time of clinical appearance of involved cervical lymph nodes is probably a function of the degree of malignancy of the tumor and, hence, is a valuable prognostic index.

4. *Clinical Stage of Cervical Lymph Nodes at Time of Surgical Treatment* (*Table* XII). Here also we have used the classification proposed in 1962 by the American Joint Committee on Cancer Staging:

N0—no clinical evidence of lymph node metastases
N1—unilateral movable lymph nodes
N2—bilateral or contralateral movable lymph nodes
N3—fixed lymph nodes (unilateral or bilateral)

Because it has not been our policy to do "prophylactic" neck dissections, we have among our 291 surgically treated cases only 10 in the N0 category. One of these died of extraneous disease, while 6 others were alive at 5 years from the time of admission. The largest category, N1, contained 187 cases with a net 5 year survival rate of 37.9 per cent. Operation was done on only 14 cases with bilateral or contralateral movable lymph nodes, *i.e.*, N2; 5 (35.7 per cent) were alive at 5 years. By contrast only 7 of 69 patients whose lymph nodes were described as "fixed" (N3) survived 5 years, a net survival rate of 10.8 per cent.

It would appear that as long as the neck lymph nodes remain mobile a reasonable salvage can be obtained by surgical treatment Operating on patients with fixed lymph nodes produces few dividends.

5. *Initial Treatment of Neck Lymph Nodes* (*Table* XIII). In 228 cases the initial treatment to neck lymph nodes was by surgery only; the net five year survival rate from the time of admission was 34.9 per cent, from the last operation 29.3 per cent.

Table XI

NET 5 YEAR SURVIVAL RATES BY TIME OF APPEARANCE OF INVOLVED LYMPH NODES IN CASES OF ORAL CANCER RECEIVING SURGICAL TREATMENT TO NECK AREA (1942–1956)

Time of Involved Lymph Nodes	Total No. of Cases	Total Alive at 5 Years	Net Survival Rate (%)
On admission	119	20	17.7
1–11 months from admission	78	25	33.3
1 year or more after admission	48	23	51.1
All Cases	245*	68	29.2

* Excludes 29 cases with "negative" lymph nodes plus 17 cases with time of appearance of lymph nodes not stated.

In 32 cases, generally at the request of the surgeon, irradiation to the neck area was undertaken after surgical treatment. The survival rate, from the time of admission was 29.0 per cent, postoperatively 22.6 per cent. These cases were probably considered unfavorable or the operation unsatisfactory; the relatively good results suggest that postoperative irradiation was beneficial.

When irradiation was the first treatment given to the neck lymph nodes and surgery was employed later, only 5 (16.7 per cent) of 30 determinate cases were alive at 5 years from registration and only 3 (10.0 per cent) survived 5 years following operation. This group contained many unfavorable cases; preoperative irradiation does not appear to have been strikingly effective in improving their prognosis after neck dissection.

6. *Type of Operation* (*Table* vi). In the group of 184 patients treated by unilateral standard radical neck dissection, there was a net 5 year survival rate of 31.6 per cent and a postoperative 5 year survival rate of 26.9 per cent.

Upper neck dissection was employed in 35 cases where involved lymph nodes seemed to be confined to the upper neck and the patient was judged a poor operative risk. The net 5 year survival rate was 26.5 per cent and the postoperative 5 year survival rate 23.5 per cent. Neck lymph node recurrence developed in 19 patients (54.3 per cent). It is probable that in some this might have been avoided if complete radical neck dissection had been carried out. In recent years upper neck dissection is performed only rarely.

Table XII

NET 5 YEAR SURVIVAL RATES BY CLINICAL STAGE OF LYMPH NODES AT TIME OF OPERATION ON NECK AREA (1942–1956)

Category	Total Cases	Total Alive at 5 Years	Net Survival Rate (%)
N0	10	6	†
N1	187	67	37.9
N2	14	5	35.7
N3	69	7	10.8
Not Stated	11	4	36.8
All Cases	291	89	32.2

† Rate not calculated for fewer than 10 cases.

Table XIII

NET 5 YEAR SURVIVAL RATES BY INITIAL TREATMENT OF LYMPH NODES IN CASES OF ORAL CANCER RECEIVING SURGICAL TREATMENT TO NECK AREA (1942–1956)

Initial Treatment of Neck Lymph Nodes	No. of Cases Treated	Net 5 Year Survival Rates	
		From Admission (%)	From Last Operation (%)
Surgery only	228	34.9	29.3
Surgery followed by irradiation	32	29.0	22.6
Irradiation followed by surgery	31	16.7	10.0
All Cases	291	32.2	26.4

The results obtained in 48 "combined" operations (Table vii) have been described above.

7. *Surgical Judgment and Technique.* Of the 291 patients receiving surgical treatment to the neck lymph nodes, 112 (40 per cent) were operated on by the senior author (Table xiv). Forty-nine of these were alive at 5 years from the time of admission, a net survival rate of 47.6 per cent. Forty-one lived at least 5 years after their most recent operation, a net postoperative survival rate of 39.8 per cent.

These results contrast favorably with the equivalent rates for the other 179 cases in the series, *i.e.*, 23.1 per cent net 5 year survival from the time of admission and an 18.5 per cent net postoperative 5 year survival rate.

It is suggested that the surgeon's judgment in selection of cases for operation and in choosing the appropriate procedure are of great importance, along with his skill and experience, in influencing the survival rate following operations for oral cancer and its complications.

BILATERAL RADICAL NECK DISSECTIONS

There were 2 five year postoperative survivors from among 6 patients who underwent simultaneous bilateral radical neck dissection. In 18 other cases a radical dissection on the second side was done sometime after the original operation. From these, there were 4 who survived at least 5 years following the last operation. Thus, for the entire group of 24 cases with bilateral neck dissections, all of which had pathologically positive lymph nodes, there was a net 5 year postoperative survival rate of 25 per cent. This justifies the application of such extensive operative therapy in carefully selected cases.

COSMETIC AND FUNCTIONAL RESULTS OF NECK DISSECTION

In all radical neck dissections for metastatic squamous cell cancer, we remove the sternomastoid muscle and do a complete clearance of the anterior and posterior triangles including the submental triangle. We use only sharp dissection proceeding along anatomic planes with precise indentification of all important structures. Blood is replaced as it is lost, the amount monitored by weighing sponges. When major lymph ducts are divided, they are carefully ligated with fine silk.

We attempt to minimize cosmetic disability. Incisions are varied with skin creases being used wherever possible and straight vertical scars avoided because of their tendency to contracture. Accurate closure is obtained by closely placed interrupted sutures of oooo silk. Suction drainage has been routinely used for more than 10 years; it is so effective that no dressing and no tight bandages are required.

We have always been attracted to the idea of preserving the spinal accessory nerve Included in the present series are 12 cases in which this was done—all operated on by the senior author and all with positive lymph nodes. Seven are living and well more than 5 years since operation, including 1 patient who had a simultaneous bilateral dissection with both accessory nerves being saved. Of the 5 who did not survive, 1 died of extraneous disease, 1 of distant metastases, and 1 of recurrent primary tumor, all without further neck lymph node involvement, while a fourth patient died with uncontrolled contra-

Table XIV

NET 5 YEAR SURVIVAL RATES IN PERSONAL CASES OF ORAL CANCER RECEIVING SURGICAL TREATMENT TO NECK LYMPH NODES (1942–1956)

Operative Procedure	No. Treated	Total Alive at 5 Yeras	Net 5 Year Survival (%)	5 Year Postoperative Survival	
				No.	Net (%)
Unilateral radical neck dissection	54	25	51.0	21	43.0
Unilateral upper neck dissection	10	4	40.0	4	40.0
Combined excision of primary lesion plus neck dissection	31	13	46.4	11	39.3
Other operations	17	7	43.8	4	25.0
All Personal Cases	112	49	47.6	41	39.8
All Other Cases	179	40	23.1	32	18.5
All Cases	291	89	32.2	73	26.4

lateral disease of the lymph nodes. In only 1 of the 12 cases was there recurrence in the dissected area.

These results have encouraged us to extend to an increasing number the policy of sparing the spinal accessory nerve in selected cases—those who: (a) have no detectably involved lymph nodes along the course of the nerve, (b) because of age or occupation have a special need for normal shoulder function, and (c) are unlikely to suffer from a slight prolongation of operating time. The cosmetic and functional benefit is great. These patients are very much better off than those who, following the standard operation, have winging of the scapula, atrophy of the trapezius, and limitation of shoulder movement.

DISCUSSION

In a large series of oral cancer cases, we have examined those aspects of management which are related to involvement of cervical lymph nodes. Our findings have significance only in the context of the treatment policy which has governed this management—briefly stated, radiation to the primary tumor, surgery for the neck lymph nodes.

The virtue of this policy is that many patients, in whom it would be either unnecessary or unavailing, are spared the disfigurement and disability which may follow major cancer surgery in this area. Its chief defect, we now believe, is the development of a sort of therapeutic schizophrenia, an arbitrary and artificial separation of the treatment of the primary disease from that of its "secondaries." Indeed, this symposium stands as evidence that such separation can be viewed with equanimity in a forum which should vigorously reject it. The truth is that we must all, radiotherapists and surgeons, try much harder in each patient with oral cancer to view the disease as a whole and to integrate its management at every stage from this broad standpoint.

We, therefore, decline to draw conclusions about "the management of involved neck lymph nodes," but offer instead a unified approach to oral cancer in all its aspects.

We feel that radiation therapy is the method of choice for the initial treatment of most squamous cell cancers in the mouth. Favorable cases will in many instances be thus simply cured while others, more advanced or more aggressive, will be arrested or alleviated temporarily. If, however, at any time after the initial "curative" course of irradiation, the tumor persists or recurs, surgical excision is indicated. Repeated courses of irradiation are not advised except for lesions judged inoperable or in patients unsuitable for major surgery. When one therapeutic agency has proven inadequate, the alternative should be offered at once.

When involved neck lymph nodes are detected in the absence of demonstrable distant spread, operation is mandatory unless the lymph nodes are fixed, the primary unresectable, or the patient a bad risk. Enlarged lymph nodes felt on admission should be kept under observation until irradiation of the primary growth has been completed and its effect observed. If the neck lymph nodes disappear, one may watch and wait; if they remain palpable, surgical intervention is required.

In major operations for oral cancer, both primary site and areas of lymphatic spread should generally be dealt with together. Thus, when excising recurrent primary disease, the operation should be extended to include neck dissection. Similarly, when neck dissection is undertaken to deal with involved lymph nodes, the primary site should in most cases be widely removed even though it may appear to be controlled by previous irradiation. Separate treatment of primary and secondary tumor is no more rational in this area than with malignancies elsewhere.

SUMMARY AND CONCLUSIONS

One thousand, one hundred and seventy-seven cases of squamous cell oral cancer have been studied with particular reference to those aspects of management related to involvement of the cervical lymph nodes. The general policy governing treatment has been irradiation of the primary lesion and surgery for the secondary disease in the neck. This produced an over-all net 5 year survival rate from the time of admission of 38.1 per cent.

Just under one-half (46.4 per cent) remained free of lymph node involvement; of these 64.2 per cent lived 5 years. For the group with spread to the neck lymph nodes (53.6 per cent), the survival rate was only 20.4 per cent. When lymph nodes were involved on admission, the survival rate was 15.0 per cent; for those in whom enlarged lymph nodes were detected later, the rate was 27.8 per cent.

In 257 cases with lymph node involvement treated only by irradiation, the net survival rate was 11.7 per cent.

Surgical treatment to neck lymph nodes was undertaken in 291 cases, producing a net survival rate of 32.2 per cent.

The operative procedure in 242 cases involved the neck only (radical neck dissection 194, upper neck dissection 35, local excision 13). The removed lymph nodes were "positive" in 91.8 per cent. There were 11 operative deaths (4.5 per cent). The net 5 year survival rate from the time of admission was 31.6 per cent, from the last neck operation 26.4 per cent.

Combined excision of the primary tumor plus neck dissection was done in 48 cases, 38 by in-continuity procedures. The lymph nodes were "positive" in 70.8 per cent. There were 5 postoperative deaths (10.4 per cent). The net 5 year survival rates were from the time of admission 36.4 per cent, from the last operation 27.3 per cent.

In cases selected for surgical treatment to the neck lymph nodes, our best results have been with carcinoma of the floor of the mouth, our poorest with gingival lesions. Survivorship was significantly better in those who on admission had small primary lesions (T1) than in those with more advanced tumors. As long as involved lymph nodes were mobile (N1, N2), reasonably good results were obtained from surgical treatment. In cases with fixed lymph nodes (N3), only 1 in 10 survived 5 years.

Evidence is presented that surgical judgment and technique may be important factors in influencing the results obtained from operative treatment to the neck lymph nodes. In a personal series of 112 cases, comprising 40 per cent of the total surgical group, it was possible to achieve 5 year survival rates of 47.6 per cent from the time of admission and 39.8 per cent from the last operation.

There were 24 patients who had bilateral radical neck dissections; in 6 the operation was a single (simultaneous) procedure. All 24 had positive lymph nodes. Six (25 per cent) lived 5 or more years after the most recent operation.

Included in the series are 12 patients with positive lymph nodes who underwent neck dissection modified by preservation of the accessory nerve. Seven are living and well more than 5 years after operation. In only 1 of the 12 cases has there been recurrence in the dissected area.

Regrowth of the primary tumor has been the most common cause of failure in cases receiving surgical treatment to the neck lymph nodes. The apparent control of the intraoral lesion by irradiation is often merely a temporary arrest. We, therefore, now feel that, as a rule, whenever neck dissection is indicated the primary lesion should at the same time be widely removed.

As a result of this study we have found no reason to change our opinion that radiation therapy is the method of choice for the initial treatment of most squamous cell cancers in the mouth. When, however, there is residual or recurrent disease, irradiation should not be repeated unless surgical excision is contraindicated. Spread of disease to the neck lymph nodes demands neck dissection unless the lymph nodes are fixed, the primary lesion is unresectable, or the patient is a bad risk. In major operations for oral cancer, both the primary site and areas of lymphatic spread should generally be dealt with together.

Robert A. Mustard, M.D.
280 Bloor Street West
Toronto, Ontario, Canada

The authors are grateful to Dr. Clifford Ash, Director of the Ontario Cancer Institute, for permission to study the case records which have all been transferred to that institution. Our warmest thanks go to Mrs. Shirley Gordon and Miss Mary McCartney of the Records Department of the Institute who prepared the punchcards, carried out all statistical analyses, and were helpful in many other indispensable ways.

REFERENCES

1. Ash, C. L. Oral cancer: twenty-five year study. Janeway Lecture, 1961. Amer. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *87*, 417–430.
2. Wookey, H., Ash, C., Welsh, W., and Mustard, R. A. Treatment of oral cancer by combination of radiotherapy and surgery. *Ann. Surg.*, 1951, *134*, 529–540.

* * *

METASTASES IN CERVICAL LYMPH NODES FROM OROPHARYNGEAL CARCINOMA*

TREATMENT AND RESULTS

By R. H. JESSE, M.D., *and* GILBERT H. FLETCHER, M.D.
HOUSTON, TEXAS

THE majority of patients with squamous cell carcinoma of the oropharynx have clinical evidence of metastases in the cervical lymph nodes at their first observation by a physician. Since metastases in these structures have not been successfully controlled by either surgery or irradiation, the two methods of treatment have been combined at the M. D. Anderson Hospital and Tumor Institute. The merits of this approach have been reflected in better control of the lymph node metastases and improved survival rates.

In this study, the records of 267 previously untreated patients who received treatment for carcinoma of the oropharynx from 1952 through 1959 were reviewed. Of these, 158 had metastases to the cervical lymph nodes. As shown in Table I, the incidence of clinically positive cervical lymph nodes was highest (72 per cent) in patients with cancer at the base of the tongue and lowest (45 per cent) in those with palatal cancer. In reported series, approximately 80 per cent of the patients with squamous cell carcinoma of the base of the tongue were found to have metastases to the cervical lymph nodes at their first observation.[1,2,8,9] Fletcher and MacComb[6] also noted that cancer of the oropharynx proper has a greater propensity to metastasize to the cervical lymph nodes than cancer of the palatine arch, *i.e.*, palate and tonsillar pillar-retromolar trigone. Judging from the size and multiplicity of the metastases to the cervical lymph nodes at the initial examination of the patients, it is clear that carcinomas of the base of the tongue, pharyngeal wall and tonsillar fossae are more aggressive than those in the palate, tonsillar pillar and retromolar trigone (Table II). Of 99 patients with cancer of the palatine arch, 53 had clinical evidence of metastases in the cervical lymph nodes. Of these 53, 21 (40 per cent) had metastasis in only 1 lymph node. By comparison, 26 of 105 (25 per cent) of those with cancer of the oropharynx proper, had a single lymph node metastasis. The explanation probably lies in the fact that cancers of the palatine arch are discovered at an earlier stage of development. First, the palatine arch contains a larger number of pain fibers, and lesions in this location exhibit symptoms while still small. Second, the cancers can be seen by the patient. As shown in Table III, over 60 per cent of lesions of the arch were less than 5 cm. (T_1 and T_2) upon admission of the patients, whereas only 40 per cent of the oropharyngeal tumors were observed at this stage. Since the size of the primary tumor and the size and number of metastatic lymph nodes are related, patients with cancers of the palatine arch have fewer and smaller metastases to the lymph nodes when first observed by the physician than patients with cancers of the oropharynx proper.

Schulz *et al.*[12] recently reported that 22 per cent of 259 patients who had squamous cell carcinoma of the palatine arch survived 3 years. Thirty per cent of the patients who had no clinically apparent metastases to the lymph nodes and 21 per cent of those who had a single metastasis survived. Five year survival rates of 10 to 27 per cent have been reported in studies of carcinoma of the base of the tongue.[1,2,8,9] In

---

* From the University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas.

Presented at the Forty-fifth Annual Meeting of the American Radium Society, April 1-4, 1963. Part of the Symposium: Management and End Results in the Treatment of Metastatic Cervical Lymph Nodes; Chairman, Dr. William S. MacComb, Houston, Texas.

Table I

267 CARCINOMAS OF THE OROPHARYNX

Sites of Primary Tumors and Incidence of Metastases to Cervical Lymph Nodes

Primary Site	No. of Patients	No. with Metastases to Lymph Nodes
Palate	22	10 (45%)
Tonsillar pillar, retromolar trigone	77	43 (56%)
Tonsillar fossa	45	26 (58%)
Pharyngeal wall	48	25 (52%)
Base of tongue	75	54 (72%)
Total	267	158 (60%)

studies of cancer of the tonsil, an average 5 year survival rate of 19 per cent has been quoted; of the patients who presented no clinical evidence of metastasis upon admission to the hospital, 35 per cent survived 5 years.[4,5,10] Betch and Croll[3] reported a 3 year survival rate of 13 per cent among patients with squamous cell carcinoma of the oropharyngeal walls. Few figures on survivals of patients with these tumors have been published.

ANATOMY OF OROPHARYNX

Perusal of the literature reveals that not all authors agree as to the precise anatomic components of the oropharynx. In our opinion, the anterior tonsillar pillar and retromolar trigone, faucial tonsil, soft palate, base of the tongue, the vallecula, and the lateral and posterior pharyngeal walls comprise the oropharynx. The pharynx may be divided by the hyoid bone into the oropharynx and hypopharynx. As thus defined, the oropharynx has two embryonic derivations: the anterior faucial pillar, retromolar trigone, and the mucosa covering the soft palate are derived from the primitive oral cavity, whereas the tonsillar fossae, the base of the tongue, the pharyngeal walls, and the muscle of the soft palate are derived from the primitive pharynx.

STAGING OF CANCERS

At the first visit of these patients to the hospital, the primary oropharyngeal cancer and the metastases to the cervical lymph nodes are classified clinically according to a T and N system of staging, which is similar to that recommended by the International Committee for Stage Grouping in Cancer. This system has a threefold purpose: (1) the results of studies of similar groups of patients can be reported, (2) the effectiveness of treatment can be evaluated, and (3) the prognosis for any individual patient can be reasonably predicted. The clinical evaluation of the primary tumor (T) is subject to error, and even more uncertain is the clinical evaluation of the cervical lymph nodes (N). Also, the T and N system does not take into account the differences in the aggressiveness of some squamous cell cancers. Nevertheless, the size of

Table II

158 CARCINOMAS OF THE OROPHARYNX

Stages of Metastases to Cervical Lymph Nodes

Primary Site	No. of Patients	N_1 Metastases	N_2 or N_3 Metastases
Palate	10	4 (40%)	6 (60%)
Tonsillar pillar, retromolar trigone	43	17 (40%)	26 (60%)
Tonsillar fossa	26	7 (27%)	19 (73%)
Pharyngeal wall	25	5 (20%)	20 (80%)
Base of tongue	54	14 (26%)	40 (74%)
Total	158	47 (30%)	111 (70%)

Table III

STAGES OF 267 PRIMARY CARCINOMAS OF THE OROPHARYNX

Primary Site	No. of Patients	Stages T_1–T_2	Stages T_3–T_4
Palate	22	17 (77%)	5 (23%)
Tonsillar pillar, retromolar trigone	77	47 (61%)	30 (39%)
Tonsillar fossa	45	21 (47%)	24 (53%)
Pharyngeal wall	48	20 (41%)	28 (59%)
Base of tongue	75	26 (35%)	49 (65%)
Total	267	131 (49%)	136 (51%)

the primary lesion and its propensity for metastasizing usually can be fairly well correlated. The staging of the cancers (T) and the lymph nodes (N) is as follows:

T_1—Tumors less than 3 cm. in diameter
T_2—Tumors 3 to 5 cm. in diameter, with minimal extension to adjacent structures
T_3—Tumors more than 5 cm. in diameter, with limited or moderate extension to adjacent structures
T_4—Massive primary tumor
N_0—No clinical evidence of lymph node metastasis
N_1—Single clinical lymph node metastasis less than 3 cm. in diameter
N_2—Single lymph node metastasis over 3 cm. in diameter, or multiple ipsilateral metastases
N_3—Large lymph node metastasis with fixation, or bilateral metastases

TREATMENT

The treatment for metastases to the cervical lymph nodes depends upon the pattern of spread, which, in turn, depends upon the site and size of the primary tumor and its histologic type. Squamous cell carcinomas of the oropharynx are of two types: (1) the keratinizing carcinoma of the palatine arch, its pattern of spread being similar to that of cancers of the oral cavity from which its mucosa is derived; and (2) the anaplastic tumors of the tonsillar fossa, base of the tongue and oropharyngeal wall, which involve the cervical lymph nodes more extensively.

Basically, several considerations determine the choice between radical neck dissection and extensive irradiation, or both: (1) Radical neck dissection effectively controls metastases to the cervical lymph nodes from keratinizing squamous cell carcinomas, provided the lymph nodes are of moderate size and are not fixed to the skin or vital structures. (2) If the lymph nodes are large, fixed or multiple, local recurrence after neck dissection is much more likely. (3) Anaplastic squamous cell carcinomas are usually more radiosensitive than the keratinizing tumors. Also, they diffusely invade the lymph nodes, often on both sides of the neck. (4) Irradiation of the whole neck, even with moderate doses (5,000 rads over 5 weeks), can sterilize microscopic squamous cell carcinoma in small lymph nodes since few malignant cells are present and the lymph node has normal oxygenation. On the contrary, large lymph nodes contain many metastatic cells and are poorly oxygenated; thus, they cannot be sterilized and often can only be reduced in size by irradiation. The addition of further radiation to the lymph nodes, moreover, does not always prevent regrowth of the cancer. (5) A previous analysis has shown that metastases seldom invade new lymph nodes in electively irradiated areas.[11]

In view of the foregoing facts, the following general treatment has been developed: (1) Elective or prophylactic neck dissection is omitted if the neck is clinically normal. (2) A single clinically positive lymph node (N_1) adjacent to a primary lesion of the palatine arch is included in the radiation field of the primary lesion. If the lymph node is lower in the neck, a restraining dose of radiation (8×500 rads) is delivered through a separate portal. Four to 6 weeks later, a radical neck dissection is performed. (3) Multiple, fixed, or bilateral enlarged lymph nodes associated with cancer of the palatine arch or pharyngeal wall are irradiated with moderate doses (5,000 rads over 5 weeks), the whole neck usually being included. With the possible exception of a lymph node which remains fixed after delivery of the moderate dose, no further radiation therapy is administered in an effort to sterilize these lymph nodes. If the primary tumor is considered sterile, radical neck dissection is performed at 6 weeks. (4) All patients with anaplastic carcinoma of the tonsillar fossa and base of the tongue receive irradiation to the entire neck. In the presence of metastasis to a small single lymph node or to small multiple lymph nodes, operation on the neck is omitted. If the lymph nodes are large, fixed (N_3) or uncontrolled by irradiation, however, a radical neck dissection is usually performed; no attempt is made to control the tumor by the addition of local radiation. Occasionally, radical neck dissection is inadvisable because of too extensive metastases or the poor condition of the patient; in such cases, further radiation therapy is administered. The detailed plan of treatment for tumors in each anatomic site is given below.

Palate, Tonsillar Pillar and Retromolar Trigone

N_0 —6,000 rads to neck only through field covering primary lesion; no operation

N_1 —6,000 rads to ipsilateral upper neck through primary field; if lymph node is low, 4,000 rads (500×8) through separate portal; neck dissection 6 weeks later

N_2—N_3—6,000 rads to upper neck bilaterally; 5,000 rads to lower neck bilaterally; 6 to 8 weeks later, neck dissection alone or combined with resection of the primary site if indicated by the status of the latter

Tonsillar Fossa

N_0 —6,000 rads to ipsilateral upper neck

N_1 —6,000 rads to upper neck bilaterally; 5,000 rads to ipsilateral lower neck; neck dissection only for residual lymph nodes

N_2–N_3—6,000 rads to upper neck bilaterally; 5,000 rads to lower neck bilaterally; 6 to 8 weeks later, neck dissection alone, or combined with resection of the primary site if indicated by the status of the latter

Pharyngeal Wall

N_0 —6,000 rads to primary tumor and jugular lymph nodes through bilateral narrow portals

N_1 —6,000 rads to primary tumor and jugular lymph nodes through bilateral narrow portals; neck dissection if primary cancer controlled

N_2–N_3—6,000 rads to whole neck; neck dissection if primary cancer controlled

Base of Tongue

N_0 —6,000 rads to upper neck bilaterally, in conjunction with irradiation of primary lesion

N_1 —6,000 rads to upper neck bilaterally; 5,000 rads to lower neck bilaterally; neck dissection after 6 weeks for residual lymph node metastases

N_2–N_3—6,000 rads to upper and lower neck bilaterally; unilateral radical neck dissection for residual metastases if primary cancer controlled

A radical neck dissection should be performed after the primary cancer has been controlled by irradiation; this is usually 6 to 8 weeks later. If control of the primary cancer is doubtful at the time radical neck dissection is contemplated, a specimen should be removed for frozen section examination, the surgeon being prepared to remove both the primary tumor and the cervical lymph nodes in continuity. In view of the skin-sparing effect of supervoltage therapy, neck dissection following a therapeutic dose of as much as 6,000 rads is not technically difficult, and healing may be expected if no build-up material or tangential portals are used. The size of the portals for irradiation of the neck appears to have little influence upon healing. The general condition of the patient at the time of neck dissection, however, is extremely important. Often, following irradiation, the patient is unable to eat for a long time, and thus loses weight and even has a negative nitrogen balance. In the presence of a negative nitrogen balance, the operation should be postponed until the condition has been corrected.

If the patient is in poor general health, or has lost weight, or has received a radiation dose of more than 6,000 rads, a modified incision is preferable for radical neck dissection. This incision is an inverted "L," beginning at the tip of the mastoid process, continuing inferomedially to the tip of the hyoid bone, thence inferolaterally to bisect the clavicle. Thus, two skin flaps are formed instead of the usual three, and intersecting incisions over the carotid artery are avoided. All lymph nodes, with the exception of those in the submental area, can be removed easily through this incision; the submental lymph nodes are excised with some difficulty. This modified incision has always healed. After extensive radiation therapy, the procedure which is most often followed by nonhealing of the wound is resection of the primary lesion combined with radical neck dissection, in that an intraoral or intrapharyngeal suture line is necessary. Ten per cent of the deaths in this series were attributable to complications of treatment, of which nonhealing of the wound and consequent exposure and rupture of the carotid artery were the most prevalent.

As a result of these complications, the treatment for carcinoma of the oropharynx has been changed slightly. Currently, after administration of 5,000 rads to the primary site, the sensitivity of the tumor to irradiation is evaluated by measurement of its regression. If the regression is not adequate, no further irradiation is administered. After 4 to 8 weeks the primary site is excised and an ipsilateral radical neck dissection is performed at a single operation.

RESULTS

The treatment of only those patients who were alive and free of cancer at the end of 3 years was considered successful. If the patient was living with the disease or was dead from any cause at that time, the treatment was considered a failure. Some of the patients, however, had distant metastases at their first observation and were treated solely for palliative purposes. The results of the entire group of 267 patients are shown in Table IV, being based upon actual count.

The 3 year survival rate varied from 33 per cent of the patients with cancer of the pharyngeal wall to 55 per cent of those with palatal cancer. The average of the entire group was 42 per cent. Of special interest were the survival rates according to the classification of the lymph nodes. Sixty per cent of the patients without evidence of lymph node metastasis (N_0) upon admission and 46 per cent of those with a small single metastasis (N_1) survived the 3 year period Surprisingly, 37 per cent of the patients with multiple ipsilateral lymph node metastases (N_2) survived 3 years. Of

TABLE IV

267 CARCINOMAS OF THE OROPHARYNX

Three Year Survival Rates Based on Stages of Metastases to Cervical Lymph Nodes

Primary Site	N_0	N_1	N_2	N_3	Total
Palate	6 of 12	3 of 3	1 of 2	2 of 5	55%
Tonsillar pillar, retromolar trigone	24 of 34	6 of 17	8 of 16	0 of 10	49%
Tonsillar fossa	13 of 19	4 of 7	3 of 11	1 of 8	47%
Pharyngeal wall	10 of 23	1 of 5	4 of 10	1 of 10	33%
Base of tongue	13 of 21	7 of 14	2 of 10	4 of 30	35%
					Average
Total	60%	46%	37%	13%	42%

Table V

267 carcinomas of the oropharynx

Combined Dissection and Radiation Therapy for Metastases to Cervical Lymph Nodes; 3 Year Survivals

Total no. of patients surviving 3 years		113
Planned combined treatment	23	
Operation for residual or recurrent lymph node metastases	18	
Total	41	

those with either fixed or bilateral lymph node metastases (N_3), only 13 per cent lived 3 years.

The effectiveness of combined irradiation and surgery is exemplified by the fact that of the 113 surviving patients, 41, or approximately 36 per cent, received this type of treatment (Table v). This number represents almost all the surviving patients who had metastases to the cervical lymph nodes at some time during the course of their disease. Twenty-three of the group had irradiation and immediate neck dissection, while 18 had irradiation, and a neck dissection was performed later for residual or recurrent disease.

Fatalities. Of the 267 patients, 154 expired (Table vi). Of these, 62 had an uncontrolled primary cancer. Only 13 of the 62 had a lesion less than 5 cm. in diameter, while 49 had a lesion larger than 5 cm. Approximately one-fourth of the patients were treated with orthovoltage equipment. Since supervoltage therapy became available in this institution, the incidence of uncontrolled primary cancer has decreased.[7]

Sixteen fatalities were attributed to uncontrolled metastases to the cervical lymph nodes after the primary cancer had been controlled. In the majority of these patients, the lymph node metastases were originally classified as advanced. On review of the records of the 16, however, it was obvious that 6 could have survived longer if neck dissection had been performed within 8 weeks after completion of the radiation therapy. Most of these patients were treated before radical neck dissection was adopted as a part of the planned treatment.

Distant metastasis was responsible for 24, or approximately one-sixth, of the fatalities. As the cancers were better controlled locally and regionally, more patients lived longer and the number with metastases below the clavicle increased.

Seven per cent of the patients expired of a new primary cancer, chiefly in the lung or esophagus. That over 10 per cent died of intercurrent disease is explained by the fact that many patients of the group were elderly and were afflicted with other infirmities.

SUMMARY

Metastasis to the cervical lymph nodes of patients with oropharyngeal cancer is usually present at their first observation by the physician. For such patients a systematic treatment, based upon dual staging of the primary tumor and its metastases and featuring irradiation and subsequent radical dissection of the lymph nodes, is presented. The 3 year survival rates of the patients treated by this method for cancer in various anatomic sites in the area are reported. These are significantly better than the survival rates previously quoted. Of particular interest are the survival rates of patients who had a single lymph node metastasis upon admission to the hospital

Table VI

267 carcinomas of the oropharynx

Fatalities and Causes

Primary tumor uncontrolled	$T_1-T_2=13$ $T_3-T_4=49$	62
Cervical metastases alone, uncontrolled	$N_0-N_1=4$ $N_2-N_3=12$	16
Distant metastases		24
New primary cancer		11
Intercurrent disease		17
Complication of treatment		15
Unknown		9
Total		154

(46 per cent) and multiple ipsilateral lymph node metastases (37 per cent). These successes are attributable to the cooperation of the radiotherapist and the surgeon in combining their modalities of treatment.

R. H. Jesse, M.D.
The University of Texas
M. D. Anderson Hospital and
Tumor Institute
Houston 25, Texas

REFERENCES

1. Baud, J. End results of radiotherapy of cancer of tongue. Am. J. Roentgenol. & Rad. Therapy, 1950, *63*, 701–711.
2. Beahrs, O. H., Devine, K. D., and Henson, S. W., Jr. Treatment of carcinoma of tongue; end-results in one hundred sixty-eight cases. *Arch. Surg.*, 1959, *79*, 399–403.
3. Betsch, P. C., and Croll, R. Les cancers de la paroi postérieure de l'oro et de l'hypopharynx. *J. de radiol., d'électrol. et de méd. nucléaire*, 1959, *40*, 221–229.
4. Duffy, J. J. Carcinoma of tonsil; review of 122 histologically proved cases, treated 1921–1928, inclusive. *Surg., Gynec. & Obst.*, 1932, *54*, 539–550.
5. du V. Tapley, N., Evans, R. A., Kligerman, M. M., and Jacox, H. W. Carcinoma of tonsillar area: factors influencing results of treatment. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *82*, 626–633.
6. Fletcher, G. H., and MacComb, W. S. Radiation Therapy in the Management of Cancers of the Oral Cavity and Oropharynx. Charles C Thomas, Publisher, Springfield, Ill., 1962.
7. Fletcher, G. H., and Jesse, R. H., Jr. Contribution of supervoltage roentgenotherapy to integration of radiation and surgery in head and neck squamous cell carcinomas. *Cancer*, 1962, *15*, 566–577.
8. Lederman, M. Cancer of base of tongue: treatment by radiotherapy. *J. Laryng. & Otol.*, 1959, *73*, 279–288.
9. Marcial, V. A. Carcinoma of base of tongue. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *81*, 420–429.
10. Martin, H. E., and Sugarbaker, E. L. Cancer of tonsil. *Am. J. Surg.*, 1941, *52*, 158–196.
11. Million, R. R., Fletcher, G. H., and Jesse, R. H. Evaluation of elective irradiation of neck for squamous cell carcinoma of nasopharynx, tonsillar fossa, and base of tongue. *Radiology*. In press.
12. Schulz, M. D., Lintner, D. M., and Sweeney, L. Carcinoma of palatine arch. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1963, *89*, 541–548.

THE TREATMENT OF CERVICAL LYMPH NODE METASTASES FROM CARCINOMA OF THE HYPOPHARYNX*

By LEWIS W. GUISS, M.D.†
LOS ANGELES, CALIFORNIA

THE author's modest experience in the management of hypopharyngeal carcinoma and its lymph node metastases is presented in a way to permit comparison of treatment results with those of other areas of the pharynx and intraoral cavity. An attempt has been made to develop some guide lines for treatment of these lesions based on an analysis of end results obtained for various stages of the disease. Since it is impossible to separate the treatment of lymph node metastases from that of the primary lesion in the particular area of the hypopharynx, the therapeutic approach to the primary lesion will also have to be discussed. Consideration of management of lymph node metastases without including the primary lesion would seem impractical since, whether the total therapy program be surgical or irradiation, the two problems are usually dealt with simultaneously and therefore should not be separated.

MATERIAL

All cases of epidermoid carcinoma of the hypopharynx accepted for treatment in the author's private practice for either curative or palliative management during the study period are included. Patients who were seen only for purpose of consultation, whether prior or during a course of therapy, and all those seen only for follow-up are excluded. Further, all whose pathologic diagnosis was not that of epidermoid carcinoma, *e.g.*, adenocarcinoma, lymphosarcoma and rhabdomyosarcoma, were also excluded from consideration. Only 35 patients could be included in this series who had proven epidermoid carcinoma with primary lesions originating in the hypopharynx who were accepted for treatment, either curative or palliative in intent. About 75 per cent of the patients were males; the youngest was a female, 39 years of age; the oldest, a male of 88 years of age. The median age was 60. Most patients gave histories of heavy tobacco consumption while an inordinate number appeared to be chronic alcoholics. Suicidal tendencies were frequent and together with poor general condition and intercurrent disease often prevented indicated treatment programs from being achieved.

METHOD

The clinical data were reduced as accurately as possible to common denominators and the information transferred to punch cards for analysis. To permit comparison with other papers presented in this symposium, the anatomic definitions and criteria as set forth for pharynx by the American Joint Committee on Cancer Staging and End Result Reporting are employed. The actuarial method of calculating end results while preferred did not seem appropriate for such a small series so the older method of preparing "5 year cure rates" was used.

DEFINITION OF TERMS

The stage classification for hypopharynx proposed by the American Joint Committee on Cancer Staging is a clinical one based on the anatomic extent of the primary lesion and lymph node metastases at the time of

---

* Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963. Part of the Symposium: Management and End Results in the Treatment of Metastatic Cervical Lymph Nodes; Chairman, Dr. William S. MacComb, Houston, Texas.

† Associate Clinical Professor of Surgery, School of Medicine, University of Southern California.

Table I

CLASSIFICATION OF PRIMARY LESIONS OF HYPOPHARYNX

		Pyriform Sinus	Postcricoid	Posterior Pharyngeal Wall	Total
T1	Confined to 1 Area No Fixation	12		2	14
T2	Involves 2 Sites No Fixation	12		3	15
T3	Extension beyond Hypopharynx and/or Fixation	5	1		6
	Total	29	1	5	35

the first examination prior to any treatment.

The hypopharynx is defined as extending from just above the level of the tip of the epiglottis, inferiorly to the lower border of the cricoid cartilage. It is made up of 3 distinct parts: (1) the lower posterior pharyngeal wall; (2) the pyriform sinuses; and (3) the posterior surface of the larynx or postcricoid region. The extent of the primary lesion is indicated by the usual T1,2,3 method: T1 lesions being confined to one particular anatomic area; T2 lesions extend into two sites without fixation; and T3 lesions beyond the hypopharynx with or without fixation. The classification of the primary lesions is shown in Table I. It will be noted that almost all arose in the pyriform sinus, that 14 were early, an additional 15 were moderately advanced and only 6 would be classified as advanced lesions with regard to the extent of the primary process.

The classification of lymph node metastases is the same as that for other pharyngeal areas. Again, this is a clinical classification: N0 indicates that none were palpable; N1, clinically palpable lymph nodes that were not fixed; N2, the presence of fixed lymph nodes. The term, "fixed lymph nodes," implies that the tumor had extended beyond the capsule of the lymph node and was no longer a discrete metastasis. The absence or presence of distant metastases is indicated by the terms, M0 and M1. The distribution of these cases with reference to lymph node metastases is shown in Table II. It will be noted that about one-half presented without lymph node involvement and it is probably significant that 4 of the 5 posterior pharyngeal

Table II

CLASSIFICATION OF METASTASES TO CERVICAL LYMPH NODES FROM EPIDERMOID CARCINOMA OF THE HYPOPHARYNX

	Lymph Node Status	Pyriform Sinus	Postcricoid	Posterior Pharyngeal	Total
N0	None Palpable	12		4	16
N1	Palpable Not Fixed	14 (1 case M1)	1	1	16
N2	Fixed	3			3
	Total	29	1	5	35

TABLE III

STAGING OF HYPOPHARYNGEAL CANCER

Stage			M0			M1	Total
			N0	N1	N2		
I	T1	Small Primary No Palpable Lymph Nodes	8				8
II	T2 T3	Larger Primary No Palpable Lymph Nodes	7 1				8
III	T1 T2	Favorable Primary Lymph Nodes Not Fixed		5 7			12
IV	T3	Large Primary Lymph Nodes Not Fixed		3			7
	T1 T2 T3	All Cases with Fixed Lymph Nodes			3		
	T1 T2 T3	All Cases with Distant Metastases				1	
		Total	16	15	3	1	35

wall primary lesions fell in the N0 group. An equal number had palpable but not fixed lymph nodes (one of these had distant metastases) and only 3 could be regarded as having fixed lymph nodes. In view of the small number of cases in the series, the different anatomic primary sites are combined for further consideration.

The clinical staging of these hypopharyngeal cases as defined by the American Joint Committee is a combined consideration of the extent of the primary disease and the extent of metastases. The actual staging of these cases then is shown in Table III. When the T classification of the primary is combined with the NM evaluation of regional and distant metastases, the clinical picture appears considerably less attractive, and in this small group somewhat less than one-half (16 Stage I and II cases) were considered favorable; one-third as somewhat advanced (Stage III) and the remaining 7 were usually those appropriate only for palliative programs.

TREATMENT

Inasmuch as early lymph node metastasis from hypopharyngeal cancer lies immediately adjacent to the primary lesion or at least in its near vicinity, the treatment program is usually selected to deal with the primary lesion and lymph node involvement simultaneously. Most of the patients were treated definitively by irradiation. Surgery was used initially only when it was felt that either the primary lesion or the lymph node involvement was too extensive to be successfully treated by irradiation. However, a number of patients had secondary treatment by surgery either because of uncontrolled primary disease or lymph node metastases.

IRRADIATION PROGRAM

The patients who were subjected to definitive radiation therapy received orthovoltage therapy at either 200 or 280 kv. with a half value layer of 1.7 mm. of copper. The ports were usually circular if the clinical setting was favorable, varying in diameter from 5 to 8 cm. depending upon the extent of the disease and arranged to crossfire both the primary and lymph node areas. More extensive lesions and cases treated with palliative intent were irradiated with rectangular or square ports sufficiently large to encompass the disease. Most of the patients were treated 5 days a week and were carried to tumor doses which varied between 5,000 to 6,500 r. Rarely, if there was an unusually severe biologic reaction, therapy was terminated at tumor doses below 5,000 r. Seven of the patients had to have tracheostomy either during or immediately after their treatment programs, frequently under near-emergency conditions. It appears that, if the tumor is extensive and the airway questionable, it would be more advantageous to do this electively prior to the institution of irradiation.

The sequence of the treatment programs is shown in Table IV. Five patients received only palliative management (3 with advanced disease in the neck; 1 with distant metastases and 1 with advanced intercurrent gastrointestinal carcinoma) and will not be further considered. Thirty of the 35 in the group were treated with curative intent. Of these, 27 received irradiation. It is of considerable interest that in 24 of the 27, the primary lesion was controlled. This included all 15 of the Stage I and II cases (without metastatic lymph nodes) that were treated for cure, indicating the effectiveness of such a program for control of favorable primary lesions. Of the 3 cases in which the primary lesion was not controlled by irradiation, 2 with very extensive persistent disease had laryngectomies with neck dissection and died before they left the hospital; 1 refused further therapy.

Of the 24 patients who had their primary lesions controlled by radiation therapy, 15 were in Stage I and II and so clinically had no lymph nodes to evaluate. Two of these patients subsequently developed recurrent primary lesions both of which were successfully re-treated, 1 by electrocoagulation and the other by implantation of radon seeds. Five patients subsequently developed lymph node metastases; 1 being treated successfully with laryngectomy and radical neck dissection; the other 4 did not receive additional therapy for various valid reasons, usually intercurrent disease.

Out of the 9 Stage III and IV patients (clinical evidence of lymph node metastases) who had their primary lesions controlled by irradiation, in 5 the lymph nodes regressed also and all remained free of any evidence of recurrence in the neck, either primary or to the lymph nodes. Three are now alive and free of disease while 2 have died of distant metastases. The other 4 cases in the advanced group in which the primary lesions were controlled but the lymph node metastases were not controlled fared badly. Three had radical neck dissections: 1 died subsequently of pneumonia, probably incident to an impaired airway; 1 died of brain metastases and 1 was an operative death. The remaining case with persistent lymph node metastases was not treated further because of a strong suicidal tendency.

The 3 cases that were treated primarily by surgery with curative intent were selected for this approach because of the extent of their primary lesion and the lymph node metastases. Two patients had a laryngectomy with radical neck dissection; subsequently 1 died of distant metastases, the other of intercurrent disease. The remaining patient with extensive bilateral lymph node metastases had a total laryngectomy with bilateral radical neck dissection and died later of bilateral metastatic lymph node recurrence.

END RESULTS

The 5 year end results tabulated by stage of the disease are given in Table V. It should be noted that all Stage I and II cases were treated by irradiation and that 7 of the 15, or 42 per cent, were free of disease at the end of 5 years. Of the Stage III and IV cases, numbering 16, there were but 3 5 year cures (20 per cent) and these were all

TABLE IV

SEQUENCE OF TREATMENT PROGRAMS

Primary Program						Secondary Program			
35 Total	5 Palliative	1 Intercurrent Carcinoma							
		4 Advanced or M1							
	30 Treated for Cure	27 by Irradiation	24 Primary Controlled	15 Stage I and II (no palpable lymph nodes)		2 Recurrent Primary—	1 Electrocoagulation—NED		
							1 Radon Seeds—NED		
						5 Developed Metastatic Lymph Nodes	1 Radical Neck Dissection with Laryngectomy NED		
							4 No Treatment	Coronary Occlusion Tuberculosis Inanition Bilateral Metastatic Lymph Nodes	DN
				9 Stage III and IV (with metastatic lymph nodes)	5 Lymph Node Metastases Controlled	3 NED			
						2 DM			
					4 Lymph Node Metastases Not Controlled	3 Radical Neck Dissection	DM (brain metastases) DID (pneumonia) DO		
						1 No Treatment (suicidal tendency) DN			
			3 Primary Not Controlled	2 Laryngectomy with Neck Dissection (2 DO)					
				1 No more Treatment (DT)					
		3 by Surgery	2 Laryngectomy with Radical Neck Dissection (1 DID) (1 DM)						
			1 Laryngectomy with Bilateral Radical Neck Dissection (DN)						

Code to Tables: NED=Alive, free of cancer. D=Dead or Death. DID=Death from intercurrent disease. DM=Death from distant metastases. DN=Death from lymph node metastases. DO=Operative death. DT=Death from primary lesion.

TABLE V

5 YEAR RESULTS BY STAGE OF DISEASE—EPIDERMOID CANCER OF THE HYPOPHARYNX

	Stage I—8	Stage II—8	Stage III—12		Stage IV—7		All Stages 35
Treatment for Cure by:	Irradiation 8	Irradiation 7	Irradiation 8	Surgery 2	Irradiation 4	Surgery 1	30
NED	4	3	3				10
Dead of Cancer	2 (DN)	2 (DN)	4 2 (DM); 1 (DT); 1 (DO)	1 (DM)	4 2 (DO); 2 (DM)	1 (DN)	14
Dead—Intercurrent Disease	2 1 Pneumonia 1 Alcoholism	2 Tuberculosis	1 Pneumonia	1 Coronary Occlusion			6
Palliative Management only		1	2		2		5
							Total 35

(For code see Table IV)

"Cure Rates"
Absolute 10/35=28.6%
Relative 10/30=33.3%
Determinate 10/24=41.6%

treated primarily by irradiation. The 5 year "cure rates" were surprisingly heartening. Including all cases the absolute figure was 28.6 per cent. Excluding cases treated for palliation, the relative figure rose to 33.3 per cent and the determinate rate which excludes all those who died before 5 years of intercurrent disease was 41.6 per cent. These figures on the surface appear unusually high but should not be regarded too critically because of the small number of cases in the series and the relatively high proportion of Stage I and II cases.

TREATMENT OF LYMPH NODE METASTASES

Although Stage I and II cases were by definition clinically free of lymph node involvement, despite the fact that the lymph node areas were irradiated 30 per cent subsequently developed positive lymph nodes. In 1 instance this was controlled by radical neck dissection; the other 4 cases did not have radical neck dissections because of severe intercurrent disease. Out of the patients who had irradiation to clinically evident lymph node involvement incidental to their primary lesions in the more advanced Stage III and IV, in 5 the lymph node metastases were successfully controlled by the radiation therapy although 2 subsequently died of distant metastases. In the 4 instances where the lymph node metastases did not regress, subsequent radical neck dissection produced satisfactory local results in 2 patients, but they died later, 1 of brain metastases and 1 of pneumonia; the third patient died an operative death and the fourth was not subjected to radical neck dissection because of suicidal tendencies.

THERAPEUTIC INDICATIONS

In spite of the small size of the series treated, a definite pattern of therapeutic indications seems to emerge. All Stage I and II cases should probably have a definitive radiation program directed to the primary lesion with observation of the lymph node bearing areas afterward. In those patients who develop lymph node involvement, radical lymph node dissection should be done immediately. Elective lymph node dissection would not seem to be indicated in the Stage I and II cases. In Stage III cases a primary irradiation program is indicated and in those instances with small lymph node metastases, which are brought under control, again little would be gained by adding an elective postirradiation neck dissection. However, those patients in whom the lymph node metastases are not controlled should have a complementary radical neck dissection. In all cases with persistent primary disease, immediate radical surgical intervention is in order as soon as the patient's general condition permits. The treatment of the Stage IV cases is obviously very unsatisfactory by either irradiation or surgery. In 2 instances of our series, the primary lesion was controlled but the persistent lymph node metastases could not be dissected due to the patients' resistance. Possibly the radical operative approach advocated by Wookey or the combined technique of surgery and radiation therapy suggested by Leroux-Robert might produce some improvement in the salvage rate for these patients with advanced lesions although it seems doubtful.

CONCLUSIONS

1. Stage I and II hypopharyngeal carcinomas can be successfully treated by irradiation. Neck dissection should be withheld unless there is evidence of subsequent lymph node involvement.

2. Stage III primary lesions may sometimes be cured by irradiation. Failures should be appropriately treated with radical surgery. Persistent or late lymph node metastases should be treated with radical neck dissection.

3. Stage IV results are poor with any modality. Possibly the present unsatisfactory salvage by irradiation may be improved by initial radical surgical intervention.

4. Many of the treatment failures are not due to deficiency of treatment techniques as much as to patient resistance or inability to undergo complementary surgical procedures because of poor general condition or psychologic reasons.

2009 Wilshire Boulevard
Los Angeles 57, California

END RESULTS OF TREATMENT OF CERVICAL METASTASES FROM LARYNGEAL CANCER*

By JOHN V. BLADY, F.A.C.S.
PHILADELPHIA, PENNSYLVANIA

THIS report is an evaluation of the behavior of cervical metastases from cancer of the glottic and supraglottic regions of the larynx. It is based on a study of 60 glottic and 96 supraglottic consecutive cancer cases, observed and treated from 1950 through 1957 at the Head and Neck Tumor Clinic of the Temple University Medical Center.

CLASSIFICATION AND STAGING

The clinical classification used in this report is based primarily on that reported by the Joint Committee on Cancer Staging and End Results Reporting published June, 1962, with slight modification or more exact definition (Table I).

GLOTTIC AND SUBGLOTTIC CANCER

In reviewing this material it was not possible to separate subglottic lesions as most of these involved the glottic area and the point of origin could not be ascertained. For this reason the glottic and subglottic lesions are treated as a single group. The classification and staging of these cases are shown in Table II. The incidence of cervical metastases on admission was 5 per cent.

STAGE I AND II

The Stage I group includes a total of 31 patients. Twenty-three were treated by external irradiation with a resultant 5 year salvage of 73 per cent. Eight patients were treated surgically: 4 by partial laryngectomy (laryngofissure) and 4 by laryngectomy. All 4 patients who had partial laryngectomies are 5 year survivals. Of the 4 laryngectomy cases, 1 had a recurrence and died of disease; 2 others developed cervical metastases for which a radical neck dissection was done. One of these is living and free of disease, while the other patient survived 5½ years and died of pulmonary metastasis and is considered a failure of treatment. The 5 year salvage rate for the surgically treated group is 75 per cent.

Of 57 Stage I and II cases, a total of 12 patients, or 21 per cent, developed subsequent metastases. Four of these patients had concurrent recurrent disease in or around the tracheal stoma and/or esophagus.

The time interval of clinical detection of metastases in this group of cases varied from 4 months to 5 years after treatment. In 2 cases the metastases appeared 2 and 5 years after treatment and in the remaining 10 cases the average time was 5 months.

Ten of the 12 patients were given the benefit of a radical neck dissection. Of these 10, 5 are living free of disease, 5 to 11 years. Three of the 10 had recurrent disease and metastases; in these patients in addition to the radical neck dissection, an extensive resection of the trachea and cervical esophagus was performed. Two patients died within 16 months and the third 5 years and 6 months after initial treatment. Two other patients died of distant metastases (Table III).

In 1 patient (T_1N_0) the cervical metastasis was treated by external irradiation; this patient died of disease 9 months later. In the twelfth case (T_4N_0) the metastases and recurrent disease were found to be inoperable and the patient received palliative irradiation and died 13 months later.

In analyzing the cause of death in the failure group, no definite generalizations

---

* Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1-4, 1963. Part of the Symposium: Management and End Results in the Treatment of Metastatic Cervical Lymph Nodes; Chairman, Dr. William S. MacComb, Houston, Texas.

Table I

CLASSIFICATION OF PRIMARY TUMOR

	Supraglottic Tumors		Glottic and Subglottic Tumors
T_1	Tumor 1 cm. or less confined to laryngeal surface of epiglottis, or to an aryepiglottic fold or arytenoid, or to a ventricular cavity or a ventricular band; no limitation of motion	T_1	Tumor confined to one vocal cord and mobility of cord remains normal
T_2	Tumor 1 to 3 cm. in size extending beyond the point of origin with some limitation of motion	T_2	Tumor involving both cords with normal mobility of cords, or tumor of one or both cords with fixation of cord
T_3	Extension of tumor beyond origin and involving cords with partial or complete paralysis	T_3	Tumor extending from cords either to subglottic region or to supraglottic region, *i.e.*, to ventricular bands or ventricles
T_4	Disease beyond confines of larynx and involving vallecula, base of tongue, pyriform sinuses, postcricoid area or suglottic area	T_4	Tumors as in T_1, T_2, or T_3, but with direct extension through cartilage to skin, to the pyriform sinus, or to the postcricoid region

CLASSIFICATION OF METASTASES TO CERVICAL LYMPH NODES

N_0 No clinically palpable cervical lymph node(s) (metastases not suspected)
N_1 Clinically palpable lymph nodes—movable and less than 3 cm. in size
N_2 Lymph nodes over 3 cm. in size or multiple unilateral lymph nodes
N_3 Bilateral lymph nodes
M_0 No distant metastasis
M_1 Clinical and/or roentgenographic evidence of distant metastasis

STAGING

Stage I includes T_1N_0 and T_2N_0
Stage II includes T_3N_0 and T_4N_0
Stage III includes T_1N_1, T_2N_1, T_3N_1, T_4N_1
Stage IV includes all tumors with N_2, N_3 and M_1 designations

are observed in this small series of cases. In the group treated by irradiation, 4 died of recurrent disease, 4 died of recurrence and metastases and 1 developed generalized metastases. In the surgically treated group 2 died of recurrent disease and 5 died of recurrence and metastases.

There were no salvages in the 9 irradiation failures in Stages I and II, while of the 11 surgical failures 4 patients are living free of disease 5 to 9 years after additional surgical procedures.

Table II

CLASSIFICATION AND STAGING OF GLOTTIC AND SUBGLOTTIC CANCER

Stage I	T_1N_0	27		Stage II	T_3N_0	25	
	T_2N_0	4			T_4N_0	1	
			31				26
Stage III	T_3N_1	2		Stage IV	T_3N_3	1	

Table III

GLOTTIC CANCER (1950–1957)

Stage I and II

57 Patients	
Metastases on Admission	5%
Metastases Later—(12 of 57)	21%
Neck Dissections—(10)	5 NED
3—Recurrence plus metastases	DOD
2—Distant metastases	DOD
Irradiation (1)	DOD
No Treatment—(1)	DOD

NED = No evidence of disease.
DOD = Dead of disease.

TABLE IV

SUPRAGLOTTIC CANCER (1950–1957)

Stage I

	Metastases	Metastases plus Recurrence	Bilateral Metastases	Neck Dissection	No Evidence of Disease
T_1N_0 21	11 52%	2	4	10	3
T_2N_0 4	2 50%	2	1	2	0
25	13 52%	4	5	12	3

Five year salvage in neck dissection group = 25%.

Out of 22 patients living and well over 5 years treated by irradiation, 2 developed cervical metastases and both are well and free of disease following radical neck dissection. In the group of 15 surgical successes, 3 developed cervical metastases (one bilateral) and are living and free of disease over 5 years.

STAGE III AND IV

The 2 Stage III, T_3N_1, cases were treated by combined laryngectomy in continuity with a radical neck dissection. One of these patients died of other causes 20 months later free of recurrent and metastatic disease. The second patient died of inoperable recurrent metastases in 19 months. The Stage IV, T_2N_3, patient had bilateral metastases and in spite of radical extirpative surgery, external irradiation, and implantation of radon seeds died in 6 months.

SUPRAGLOTTIC CANCER

STAGE I

A total of 21 patients classified as T_1N_0 was seen and treated (Table IV). Ten were treated by external irradiation. Five of this group survived 5 years or longer free of disease. One of these patients developed cervical metastases 9 years later for which a radical neck dissection was performed. About 1 year later a recurrence was found for which a cervical esophagectomy, resection of the base of the tongue, pharyngectomy and a year later a contralateral neck dissection were performed. The patient now has pulmonary metastases which have responded to radiation therapy. One patient died after 5 years free of recurrent or metastatic laryngeal disease from an inoperable adenocarcinoma of the stomach. Three patients were failures of treatment because of recurrent and metastatic disease. Two patients died of other causes free of laryngeal disease after 1½ and 2 years, respectively.

Of the 11 cases treated by laryngectomy with or without excision of the vallecula or the base of the tongue, only 4 survived 5 years and 1 died of heart disease 5 months after treatment. Only 2 of the 10 determinate patients did not develop subsequent cervical or generalized metastases and both are free of disease after 10 years. Five died of generalized metastases and 1 died of bronchopneumonia after surgery. The 5 year salvage is 50 per cent.

The average interval of appearance of cervical metastases was 8.2 months; the shortest was 4 months and the longest 10 years after treatment.

In this group of 21 patients, 11 developed cervical metastases (52 per cent). Three of these patients are living and free of disease after a unilateral neck dissection in 1 case and a bilateral neck dissection in 2 cases. In a fourth patient bilateral neck dissection was performed but the patient subsequently died of generalized metastases. A fifth patient with bilateral metastases had a radical neck dissection performed on one side only because of demonstrable lung metastases. Three additional patients died of generalized metastases. In 1 of these, metastases occurred 5 months after laryngectomy. Microscopic examination of the neck dissection tissue revealed capillary and vein invasion. This patient died of generalized metastases 17 months later.

Two additional patients had cervical

metastases with recurrent disease of the trachea and esophagus. Both died of disease. The eleventh case died of bronchopneumonia following a radical neck dissection.

Only 4 patients were classified T_2N_0 (Table IV). Two were treated by radiation therapy. One died of disease in 3 months and the other died of other causes 14 months after treatment.

One patient was treated by a laryngectomy and radical neck dissection in continuity. Contralateral metastases and recurrence appeared 5 months later. He died of hemorrhage from uncontrolled recurrent disease and generalized metastases. The fourth patient developed recurrent disease and metastases 32 months after a laryngectomy. A cervical esophagectomy and radical neck dissection were performed but he died of generalized disease 26 months later.

STAGE II

The T_3N_0 group contained 14 cases. Eleven were treated surgically, 2 by external irradiation and 1 refused treatment and died within 1 month (Table V).

Of the 2 patients treated by irradiation, 1 is living and well 6½ years after treatment. The other is lost to follow-up.

In the group of 11 treated surgically, 4 patients are living and well. One patient has been lost to follow-up since the laryngectomy was performed in 1952.

An elective neck dissection in continuity with largyngectomy was performed in 3 patients. None had positive lymph nodes. Two of the three subsequently developed lymph nodes in the contralateral side. One is living free of disease 8 years while the other died of generalized metastases, which appeared in the base of the neck on which an elective neck dissection was performed 39 months before.

Of the 14 T_3N_0 cases, 1 refused treatment and 2 were lost to follow-up; only 3 remained free of cervical metastases.

Eight patients had neck dissections performed, 3 of which were bilateral. In 1 of the bilateral neck dissection cases, an elective dissection was performed at the time of laryngectomy. No positive lymph nodes were found. She subsequently developed metastases in the opposite neck and died of generalized disease.

Table V

SUPRAGLOTTIC CANCER (1950–1957)

Stage II

	Metastases	Metastases plus Recurrence	Bilateral Metastases	Neck Dissection	No Evidence of Disease
T_3N_0 14	8 57%	3	3	8	3
T_4N_0 7	4 60%	4	—	4	1
21	12 57%	7	3	12	4

Five year salvage in neck dissection group = 33%.

Three of the 8 patients are living free of disease 5 years later. Of the 4 treated surgically who are living free of disease over 5 years, 3 had radical neck dissections, one of which was bilateral.

Seven patients were classified T_4N_0 (Table V). One was treated by external irradiation and developed a recurrence and cervical metastases within 6 months. A laryngectomy in continuity with a radical neck dissection was performed. Generalized metastases were noted 15 months later.

Six were treated surgically. In 1 case an elective neck dissection was done and no positive lymph nodes were found. He has remained well over 6 years. In a second case a recurrence was found in the esophagus 3 months after laryngectomy. A total cervical esophagectomy and a thyroidectomy were performed and she has remained well 6 years. In the third case, living and well, a laryngectomy and a resection of the pyriform sinus were carried out.

Three of the patients who succumbed to their disease developed recurrences and cervical metastases within 6 and 9 months

TABLE VI

SUPRAGLOTTIC CANCER (1950–1957)

Stage III

Bilateral Neck Dissection	— 4	1 NED
Laryngectomy plus Radical Neck Dissection	—13	4 NED
Irradiation plus Radical Neck Dissection	— 4	3 NED
Irradiation Alone	— 4	4 DOD
	21	

Five year survival = 35%.

NED = No evidence of disease.
DOD = Dead of disease.

after initial treatment. In the fourth case because of recurrence and metastases, a resection of the base of the tongue, pharynx, cervical esophagus and trachea in continuity with a radical neck dissection was performed. In addition, the internal carotid artery was resected and a reanastomosis was accomplished. The patient died 10 days later. At autopsy softening of the right hemisphere of the brain was found. The reanastomosed internal carotid artery was not occluded and it may be assumed that the brain damage occurred during the surgery.

STAGE III

Twenty three patients comprised the Stage III group (T_1N_1—1; T_2N_1—3; T_3N_1—7; T_4N_1—12) (Table VI). Two of these patients refused to undergo any form of treatment because of advanced disease; 1 died within 3 weeks.

Of the remaining 21, 13 were treated by laryngectomy in continuity with a radical neck dissection and whatever additional surgery was considered necessary such as partial or total pharyngectomy or esophagectomy and resection of the base of the tongue and partial thyroidectomy. Of this group 4 survived 5 or more years without recurrence or metastases. One died of other causes free of disease 4 years and 4 months after treatment.

A review of the 8 failures is of interest. In 1 case metastases occurred in the opposite neck 4½ years after treatment of the primary lesion. Following a dissection of the upper mediastinum and removal of the clavicle in continuity with a radical neck dissection, the patient died of hemorrhage due to invasion of the major mediastinal vessels 5½ years after initial treatment. In another patient a laryngectomy, thyroidectomy and a radical neck dissection were performed; however, because of extensive involvement of the carotid artery, it was deemed unwise to attempt a resection of the artery and the patient succumbed within 1 month after a hemorrhage. In the third case death was due to bronchopneumonia 1 week after surgery following a course of radiation therapy. In the fourth case two distinct primary lesions were present, one involving the entire larynx and the other the posterior pharyngeal wall. A laryngectomy and a total pharyngectomy in continuity with a radical neck dissection were performed. He died of generalized metastases within 12 months.

The remaining 4 failures were due to generalized metastases. A bilateral neck dissection was performed in 4 cases. One of these survived over 8 years.

In the group of 8 patients treated by external irradiation, a radical neck dissection was performed in 4 cases. Three of the 4 are alive. The 4 treated by irradiation alone all died, 2 of recurrence and metastases and 2 of generalized metastases.

The 5 year survival rate for Stage III determinate group is 35 per cent.

STAGE IV

Of the 27 Stage IV cases, 3 had generalized metastases when first seen and received palliative treatment. Eight of the cases had bilateral metastases (Table VII).

In 14 cases external irradiation was used for the treatment of the primary lesion. In 8 of these patients a radical neck dissection preceded or followed the completion of irradiation. Three of these survived free of disease 5 years or more. A recurrence of the primary lesion was noted after 4 months in

2 cases and after 18 months in another. Two of these cases were treated by laryngectomy with resection of the adjacent tissues and the third was given a second course of external irradiation and radium implantation. One of the cases in which laryngectomy was performed is a 10 year survival.

There were no survivors in the 6 treated by irradiation alone.

Eleven were treated by laryngectomy, partial or total pharyngectomy, and/or esophagectomy in continuity with a radical neck dissection. In 2 cases a bilateral neck dissection was performed. Three survived free of disease over 5 years and 8 died of extensive recurrence and generalized metastases.

It is to be noted that 3 of the deaths are attributed to the radical surgical procedures performed. In 1 case following completion of radiation therapy (total dose of 5,040 r), a radical neck dissection was performed and on the seventh postoperative day the carotid artery sloughed and a fatal hemorrhage occurred. In the second case the common carotid artery was resected following which the patient developed cerebral thrombosis resulting in hemiplegia and death 4 months later. The third patient died on the thirteenth postoperative day of femoral thrombosis and uremia following a laryngectomy and thyroidectomy in continuity with a radical neck dissection.

The 5 year survival rate for the Stage IV group is 24 per cent.

Table VII

SUPRAGLOTTIC CANCER (1950–1957)
Stage IV

Neck Dissections		
Laryngectomy plus Radical Neck Dissection	—11	3 NED
Irradiation plus Radical Neck Dissection	— 8	3 NED
Irradiation Alone	— 6	6 DOD
	25	
Five year survival = 24%.		

NED = No evidence of disease.
DOD = Dead of disease.

Table VIII

RESULTS OF NECK DISSECTIONS

	Total No. of Cases	Dead of Disease	No Evidence of Disease
Glottic Cancer			
Stage I and II	10	0	5
Stage III and IV	3	1	0
Total	13	1	5—40%
Supraglottic Cancer			
Stage I	12	1	3
Stage II	12	0	4
Stage III	13	1	4
Stage IV	11	0	3
Total	48	2	14—30%

SUMMARY

This evaluation of the behavior of cervical metastases from cancer is based on a study of 60 glottic and 96 supraglottic cases, consecutively observed and treated from 1950 through 1957.

The analysis utilizes a classification and staging based on the T N M system.

Of the 60 glottic cancer patients 5 per cent had metastases on admission. None survived. Twelve or 21 per cent of the remaining 57 developed metastases 3 months or later after treatment of the primary lesion. Of 10 cases treated by radical neck dissection, 5 survived. One treated by irradiation died of disease.

The 96 cases with supraglottic lesions

Table IX

ELECTIVE NECK DISSECTIONS IN SUPRAGLOTTIC CANCER

T_4N_0—1	1 NED
T_3N_0—3	2 NED
T_2N_0—1	DOD
T_1N_0—0	
5	3 NED

NED = No evidence of disease.
DOD = Dead of disease.

were classified as follows: Stage I-25; Stage II-21; Stage III-23; and Stage IV-27.

A 50 per cent salvage rate was obtained in T_1N_0 (Stage I) group. In the T_2N_0 group (Stage I) there were only 4 patients; none survived. Fifty-two per cent of Stage I group developed subsequent metastases. Of 12 cases in which neck dissections were performed, 3 survived.

Fifty-seven per cent developed metastases in the Stage II group. In 12 patients neck dissections were performed and 4 survived. The 5 year survival for the determinate group is 55 per cent and for those having neck dissections 33 per cent.

Of the 23 patients in Stage III, 4 of 13 who were treated surgically survived. Four were given radiation therapy which was preceded or followed by a radical neck dissection and 3 of these survived. Of the 4 treated by irradiation alone none survived.

In Stage IV, 8 patients were treated by irradiation of the primary lesion and a radical neck dissection; 3 survived and are free of disease 5 or more years. None survived of the 6 treated by irradiation alone. Three of 11 treated by laryngectomy in continuity with a radical neck dissection survived.

Surgical complications are serious problems in Stage III and IV cases because of the extensive radical procedures that are required.

A total of 48 patients had neck dissections performed in the supraglottic cancer group (Table VIII). Fourteen of these patients are survivors (30 per cent). The 5 year salvage rate for the 13 neck dissection cases in the glottic tumor group is 40 per cent. Of 5 cases having elective neck dissections (Table IX), only 1 patient had a positive lymph node. Three of these patients survived.

Temple University
School of Medicine and Hospital
Head and Neck Tumor Clinic
Broad and Tioga Streets
Philadelphia 40, Pennsylvania

Vol. 90, No. 5

ENDOMETRIAL CARCINOMA*

By ISADORE LAMPE, M.D.
ANN ARBOR, MICHIGAN

AT THE University of Michigan Medical Center, carcinoma of the endometrium is treated by a combination of irradiation and surgery, or by irradiation alone. This neoplasm is deemed primarily a surgical problem and is treated solely by irradiation only when inoperability exists by virtue of the extent of the neoplasm or the patient's condition. In this report the therapeutic results are reviewed in 367 patients seen from 1936 through 1956. These patients presented themselves for admission without prior specific treatment for carcinoma of the endometrium. Patients treated prior to admission and entering with recurrence or metastasis are not included. Also excluded is a small group, treated by hysterectomy alone, with diagnoses such as "atypical endometrial hyperplasia," "questionable carcinoma," "early carcinoma," and "adenocarcinoma *in situ*;" all such patients survived. Included are 26 patients who were treated solely for palliative objectives, whose planned course of treatment was not completed or who received no treatment because of advanced disease.

METHOD

Preoperative irradiation was carried out preferably by external roentgen therapy; intracavitary radium was used only when extreme obesity existed. Six weeks after irradiation a total hysterectomy (and bilateral salpingo-oophorectomy) was performed. When inoperability was suspected, radium application immediately followed the external treatment. Six weeks later, after reevaluation, hysterectomy was performed if possible; otherwise, the already administrated radiation constituted the complete therapy. Linear tandem arrangements of radium sources were employed in the uterus until 1947; subsequently, the uterine cavity was packed with multiple weak (6.66 mg.) radium sources. With the latter technique, the radium exposure dose was generally 4,000 mg. hr. after roentgen therapy and 5,000 mg. hr. when radium only was used. For the roentgen therapy 200 to 250 kv. radiation of half value layer 1.0 mm. to 2.7 mm. Cu was used. The characteristic preoperative technique consisted of 4 pelvic fields, each 15×12 cm. with 1 cm. midline separation, through which the roentgen-ray beams were directed to crossfire the uterus and upper vagina. The total dose per field varied between 2,000 to 2,600 r (air) depending on the patient's size with the uterine dose approaching 4,000 r in 3½ to 4 weeks. High energy (cobalt 60) radiation was available only in the last year of the period herein reported and was utilized in only 1 patient, and not as a preoperative measure in an operable patient.

Table I

AGE DISTRIBUTION
1936–1956

Age (years)	Per Cent
50–85	82.9
60–85	51.7
70–85	17.6

AGE DISTRIBUTION

The age distribution of the 367 patients is in accord with the reported experience that as a group these patients are older than patients with carcinoma of the cervix (Table 1). Over 80 per cent were older than 50 years, more than half were 60 or more

---

* Department of Radiology (Alice Crocker Lloyd Radiation Therapy Center), University of Michigan, Ann Arbor, Michigan.
Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963. Part o. Symposium: Preoperative Irradiation; Chairman, Dr. Milton Friedman, New York, New York.

TABLE II

FIVE YEAR SURVIVAL

Years	No. of Patients	5 Year Survivors	
		No. of Patients	Per Cent
1936–1956	367	213	58.0
1936–1945	187	101	54.0
1946–1956	180	112	62.2

years of age and 17.6 per cent were above 70 years of age.

RESULTS

Of the 367 patients, 213 (58.0 per cent) were alive 5 years after treatment (Table II). For the first 10 years, 1936 through 1945, the 5 year survival rate was 54.0 per cent (101 out of 187 patients). For the last 11 years, 1946 through 1956, a higher survival rate of 62.2 per cent was obtained (112 out of 180 patients). As shown in Table III, the incidence of Stage I, Group 1 and 2 patients (International Classification) is somewhat higher (77.2 versus 70.1 per cent) in the last 11 years compared to the first decade. It should be noted, however, that somewhat better results were obtained in the last 11 years in these comparable cases (76.3 versus 70.2 per cent). Also the form of treatment producing the best results, roentgen irradiation followed by hysterectomy (see below), was applied in a higher proportion of the Stage I, Group 1 and 2 patients in the years 1936 through 1945 (51.9 per cent as compared to 38.1 per cent for the last 11 years). These observations suggest that the higher overall 5 year survival rate of 1946 through 1956 differs significantly from that of the years 1936 through 1945.

TABLE III

INCIDENCE OF STAGE I, GROUP 1 AND 2 PATIENTS

Years	No. of Patients	Per Cent	5 Year Survival (per cent)
1936–1956	270	73.6	73.3
1936–1945	131	70.1	70.2
1946–1956	139	77.2	76.3

TABLE IV

STAGE II

1936–1956

Treatment	No. of Patients	5 Year Survivors	
		No. of Patients	Per Cent
Roentgen Rays and Radium	45	11	24.4
Radium	5	1	20.0
	50	12	24.0

The results of radiation treatment in Stage II cases (extension beyond the uterus) were not striking (Table IV), but still represent a salvage of 1 patient out of 4.

In the Stage I, Group 2 patients (lesion confined to the uterus but poor operative risk) treated by irradiation, the results obtained represent a respectable performance; 58.0 per cent 5 year survival rate when treated with external roentgen irradiation and intracavitary radium, and 51.1 per cent in the group irradiated by intracavitary radium only (Table V). The results obtained by the combination of roentgen irradiation and radium may be somewhat better than shown in the table in that 3 deaths before 5 years were intercurrent; the determinate survival rate is 61.7 per cent.

Of interest is the subsequent course of the 29 patients surviving at 5 years follow-

TABLE V

STAGE I, GROUP 2

1936–1956

Treatment	No. of Patients	5 Year Survivors	
		No. of Patients	Per Cent
Roentgen Rays and Radium	50	29	58.0
Radium	47	24	51.1
	97	53	54.6

ing combined roentgen irradiation and radium treatment. Fourteen were alive at 6⅓ to 16½ years after treatment, 11 died of other causes without evidence of neoplasm of the endometrium at 5¼ to 13⅔ years, 3 died of unknown cause at 5½ to 9½ years and 1 died of apparent extension of the endometrial cancer at 8 years. These data strongly suggest that permanent eradication is obtainable by radiation therapy.

Of major interest has been the influence of preoperative irradiation upon survival of the operable Stage I, Group I patients. The entire group of patients irradiated prior to hysterectomy (roentgen irradiation alone, roentgen irradiation plus radium, radium alone) numbers 173. At 5 years, 145 (83.8 per cent) were alive. With 8 intercurrent deaths prior to 5 years, the determinate 5 year survival rate is 87.8 per cent.

In Table VI are shown the results for the patients treated by hysterectomy preceded by roentgen irradiation plus radium and those treated by hysterectomy preceded by radium alone (5 year survival rates of 63.3 and 77.3 per cent, respectively). The 5 year survival rate for the first group (roentgen irradiation plus radium, hysterectomy) is probably higher than appears in the table since 4 intercurrent deaths are included—the determinate rate is 73.1 per cent. The difference in 5 year survival rates between the 2 groups may be less apparent than the table indicates. One may comment that the combination of roentgen irradiation and radium treatment was chosen in these patients because the possibility of subsequent inoperability was suspected. The suspicion may have been based on questionable extension beyond the corpus on physical examination, or concern because of the histopathology, or on the patient's general condition. The probability is higher that this group contained more advanced lesions than the group treated by radium only preoperatively; in the latter, the form of treatment was imposed by excessive obesity as the sole factor.

TABLE VI

STAGE I, GROUP I

1936–1956

PREOPERATIVE IRRADIATION

Treatment	No. of Patients	5 Year Survivors	
		No. of Patients	Per Cent
Roentgen Rays, Radium and Hysterectomy	30	19	63.3
Radium and Hysterectomy	22	17	77.3
	—	—	
	52	36	69.2

TABLE VII

STAGE I, GROUP I

1936–1956

PREOPERATIVE IRRADIATION

Treatment	No. of Patients	5 Year Survivors	
		No. of Patients	Per Cent
Roentgen Rays and Hysterectomy	121	109	90.1

For years our interest has centered on the results of preoperative roentgen irradiation in the operable Stage I, Group I patients. Contrary to most workers, at the University of Michigan Medical Center, preoperative roentgen irradiation has been used in preference to intracavitary radium. The high survival rate noted at the end of the first 10 year period (1936 through 1945)[4] persuaded us to continue this method of treatment. Table VII presents the survival rate for the years 1936 through 1956. Of the 121 patients, 109 were alive at 5 years, a survival rate of 90.1 per cent. It may be noted that 4 deaths before 5 years were intercurrent without evidence of recurrent or metastatic endometrial carcinoma; the determinate rate is 93.2 per cent.

DISCUSSION

Three points of interest about this group of patients merit comment: (1) the incidence of total eradication of the neoplasm in the removed uterus; (2) the fate of patients surviving at 5 years; and (3) the

Table VIII

INCIDENCE OF STERILIZATION OF CARCINOMA 1936–1956

Treatment	No. of Patients	Without Cancer in Uterus	
		No. of Patients	Per Cent
Roentgen Rays and Hysterectomy	121	34	28.1
Roentgen Rays, Radium and Hysterectomy	30	16	53.3
Radium and Hysterectomy	22	7	31.8

incidence of vaginal recurrence or metastasis.

1. In the removed uteri, the lowest incidence (28.1 per cent) of total sterilization of the carcinoma was found in those irradiated preoperatively by roentgen irradiation (Table VIII). With preoperative radium treatment, the sterilization incidence was slightly higher (31.8 per cent). The highest sterilization rate (53.3 per cent) followed the most intensive irradiation, using both roentgen irradiation and radium. Paradoxically, the lowest tumor sterilization rate (28.1 per cent) occurred in the group with the highest 5 year survival rate (90.1 per cent). One may conjecture that the preoperative roentgen irradiation was without influence on the survival rate, the latter being due solely to the operative procedure or that a dose of radiation inadequate for total tumor sterilization can obviate local recurrence, vaginal involvement and remote dissemination. In view of the fact that survival rates of solely surgical treatment generally are lower[2,3,5,6,7] and the incidence of vaginal metastases are higher (see below) than in our series, we are inclined to believe that the second conjecture is the most probable.

Of the 8 deaths due to neoplasm before 5 years in the patients treated by roentgen irradiation and hysterectomy, the removed uterus showed residual carcinoma in 7 and no neoplasm in 1, a sterilization rate of 14.3 per cent compared to 28.1 per cent for the entire group of 121 patients. But of the 87 patients with residual carcinoma, 80 (92 per cent) survived 5 years or died of intercurrent disease before 5 years without evidence of endometrial carcinoma. It becomes difficult to believe that total eradication of the neoplasm by irradiation before hysterectomy is a necessary condition for survival.

2. Follow-up information for 10 years after treatment is available on 87 patients treated by roentgen irradiation and hysterectomy from 1936 through 1951 (Table IX). For this group the 5 year survival rate was 90.8 per cent and the 10 year survival rate 80.5 per cent. Of the 9 patients dying between 5 and 10 years, only 1 patient succumbed to endometrial carcinoma, the remainder to intercurrent disease without evidence of this neoplasm.

3. Of the 121 patients treated by roentgen irradiation and hysterectomy (Table VII), 12 died before 5 years after treatment, 8 of these deaths were due to endometrial carcinoma; pelvic, abdominal, retroperitoneal extension, lumbar spine and pulmonary metastases were the various manifestations. Only 1 of these 8 patients developed vaginal metastasis postoperatively, and this metastasis was associated with recurrence in the pelvis and pulmonary metastases. No patient in this series developed isolated vaginal recurrence or metastasis. The incidence of vaginal metastasis in this group of 121 patients was 0.8 per cent.

In addition to the 367 patients reported here, for various reasons, 11 patients classified as Stage I, Group I were treated by hysterectomy without any form of preoperative or postoperative irradiation. At 5 years after treatment, 10 were alive but in 2 of these vaginal metastases appeared (1 at 1½ years, 1 at 3½ years). Radiation treatment of these metastases resulted in survival at 5 years; the surgical success rate, therefore, was $\frac{8}{11}$ or 72.7 per cent. The incidence of vaginal metastasis in this small group, 18.2 per cent, is in sharp contrast to 0.8 per cent for the group described above. Such a small group cannot serve as a proper control for the Stage I, Group I patients

Table IX

FIVE AND 10 YEAR SURVIVAL
1936–1951

Treatment	No. of Patients	5 Year Survivors		10 Year Survivors	
		No. of Patients	Per Cent	No. of Patients	Per Cent
Roentgen Rays and Hysterectomy	87	79	90.8	70	80.5
		5 Dc̄ 3 Di		1 Dc̄ 8 Di	
Determinate:		79/84=94.0%		70/76=92.1%	

treated by roentgen irradiation plus hysterectomy. It is of interest, however, that it does present a picture of vaginal metastasis incidence and surgical success rate in keeping with reports in the literature on the treatment by hysterectomy alone.[1,2,3,5,6,7]

SUMMARY

1. A 58.0 per cent 5 year survival rate was obtained in 367 patients with carcinoma of the endometrium treated by irradiation alone or by irradiation and surgery from 1936 through 1956. (a) Of the 187 patients treated from 1936 through 1945, 54.0 per cent were alive at 5 years. (b) Of the 180 patients treated from 1946 through 1956, 62.2 per cent were alive at 5 years.

2. In Stage II patients, the 5 year survival rate was 24.0 per cent.

3. In Stage I, Group 2 patients, treated by irradiation only, the 5 year survival rate was 58.0 per cent with roentgen irradiation and radium, and 51.1 per cent with radium only.

4. In Stage I, Group I patients (173), hysterectomy preceded by roentgen irradiation, roentgen irradiation plus radium, or radium only resulted in a 5 year survival rate of 83.8 per cent. (a) Hysterectomy preceded by roentgen irradiation plus radium or by radium alone (52 patients) gave a 5 year survival rate of 69.2 per cent. (b) Hysterectomy preceded by roentgen irradiation (121 patients) gave a 5 year survival rate of 90.1 per cent and a vaginal metastasis incidence of 0.8 per cent. It is suggested that preoperative roentgen irradiation to a dose eradicating the neoplasm in less than one third of the cases as determined by microscopic examination of the uteri enhances the curability by hysterectomy.

Department of Radiology
Alice Crocker Lloyd Radiation Therapy
Center
University of Michigan
Ann Arbor, Michigan

REFERENCES

1. Dobbie, B. M. W. Vaginal recurrences in carcinoma of body of uterus and their prevention by radium therapy. *J. Obst. & Gynaec. Brit. Emp.*, 1953, *60*, 702–705.
2. Grünberger, V. Über die Erfolge der operativen Behandlung des Korpuskarzinoms. *Klin. Med.*, Wien, 1950, *5*, 255–262.
3. Klosterman, G. J. Annual report on results of treatment in carcinoma of uterus. Stockholm, 1960, 12, 311.
4. Lampe, I. Combined surgical and radiological treatment for endometrial carcinoma. Proc. Second National Conference, Cincinnati, Ohio, March 1952. Published by American Cancer Society, 754–764.
5. Montgomery, J. B., Lang, W. R., Farell, D. M., and Hahn, G. A. End results in adenocarcinoma of endometrium managed by preoperative irradiation. *Am. J. Obst. & Gynec.*, 1960, *80*, 972–983.
6. Pentecost, M. P., Jr., and Brack, C. B. Carcinoma of endometrium. *South, M. J.*, 1959, *52*, 190–198.
7. Rickford, B. Treatment of carcinoma of body of uterus. *J. Obst. & Gynaec. Brit. Emp.*, 1949, *56*. 41–45.

EXPERIENCE WITH PREOPERATIVE IRRADIATION FOLLOWED BY RADICAL CYSTECTOMY FOR THE TREATMENT OF BLADDER CANCER[*]

By WILLET F. WHITMORE, JR., M.D., RALPH F. PHILLIPS, M.D., HARRY GRABSTALD, M.D., EUGENE L. BRONSTEIN, M.D., A. RANALD MACKENZIE, M.B., CH.M., *and* OMAR HUSTU, M.D.
NEW YORK, NEW YORK

CLINICAL experience with the treatment of bladder cancer by radical surgery or by radiation therapy has demonstrated the limitations of these methods. The recognition of these limitations and the possibility that the combination of these two treatment methods might prove more effective than either alone provided the major impetus for the initiation, slightly more than 4 years ago, of a program to investigate the value of such a combination in the treatment of bladder cancer. This report constitutes a review of some aspects of a selected segment of this experience.

METHODS

Patients were included in this combined, preoperative irradiation-radical cystectomy study if cystectomy was indicated and if prior irradiation, whether interstitial, intracavitary or external, did not contraindicate the planned preoperative irradiation. The latter qualification excluded a number of patients who would have been included in a comparable surgical series.

The indications for radical cystectomy in this group of cases were the same as those previously reported,[3] namely: (1) the presence of noninfiltrating or superficially infiltrating cancers, diffuse or multiple, or rapidly recurrent. Admittedly, the terms utilized in defining this indication for cystectomy are not precise and clinical judgment plays a major role in decisions relative to the advisability of cystectomy in such patients; and (2) the presence of a deeply infiltrating cancer so situated that an adequate segmental resection could not be accomplished.

The system employed in characterizing the degree of infiltration or extent of the bladder cancers in this study is the modification of Jewett and Strong's[1] method of staging suggested by Marshall[2] and illustrated in Figure 1. Tumors not infiltrating more than half way through bladder muscle are considered low stage (O, A, B1) lesions; those infiltrating more than half way through bladder muscle or into perivesical fat are considered high stage (B2, C) lesions; and those invading the substance of adjacent organs or metastatic to lymph nodes or other sites are considered metastatic stage lesions (D).

Clinical staging of the tumor was carried out in each patient prior to the start of therapy, utilizing roentgenography, endoscopy, extensive biopsy and bimanual palpation under anesthesia.

The planned irradiation program for patients who met the two criteria required for inclusion in the over-all study was to administer a tissue dose of 4,000 rads to the bladder and true pelvis in a total period of 4 to 6 weeks employing supervoltage radiation. Between 1 month and 3 months following the completion of this course of irradiation, radical cystectomy was performed, employing a surgical technique identical with that utilized in a previous surgical experience.[3] This involved, in the male patients, excision of the bladder, prostate and seminal vesicles with enveloping fat and fascia and overlying peritoneum. In the female patient, the usual operation consisted of removal of the bladder, urethra, fallopian tubes, ovaries, uterus and at least the anterior vaginal wall. In both sexes a bilateral pelvic lymph node dissection extending from the mid-portion of the common iliac arteries distally along the external iliac artery to the inguinal ligament and including the obturator, external iliac, and internal iliac lymph nodes was also performed. All parietal peritoneum of the true pelvis and much of that of the adjacent false pelvis was removed in continuity with the surgical specimen, making reperitonealization technically impossible. In a few elderly poor risk patients, lymph node dissection was either curtailed or eliminated entirely, but other features of the radical excision were retained.

---

[*] From the Urologic Service of the Department of Surgery, and the Department of Radiation Therapy, Memorial and James Ewing Hospitals, New York, New York.

Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963. Part of Symposium: Preoperative Irradiation; Chairman, Dr. Milton Friedman, New York, New York.

For the purposes of the present discussion, patients were included only if *both* preoperative radiation therapy *and* subsequent radical cystectomy were accomplished. Thus, the following groups of patients were by definition *excluded* from the present analyses: (1) some patients in whom the response to preoperative irradiation was so favorable that the original plans for radical cystectomy were abandoned; and (2) patients in whom preoperative irradiation was completed but in whom the original plans for radical cystectomy were abandoned because of the finding of bladder cancer judged to be nonresectable at the time of laparotomy.

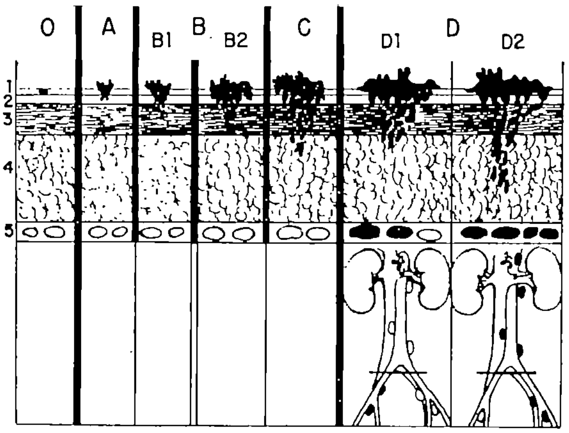


Fig. 1. Stages of vesical neoplasms: O=limited to mucosa; A=not beyond mucosa; B1=not more than halfway through muscle layer; B2=beyond the halfway level of the muscle layer but not into fat; C=beyond the muscle layer but not metastatic or invading the substance of adjacent organs; D1=metastatic to the pelvic lymph nodes and/or invading the substance of adjacent organs; D2=metastatic beyond the pelvis.

The first of these exclusions tends to create a bias adversely influencing the results of the combined irradiation surgery program by excluding patients at least potentially favorable to such a study, while the second creates a bias favorable to the results of the combined program by excluding patients with a demonstrably poor prognosis. Both of these exclusions obviously affect any comparison with a surgical series; in the first instance because cystectomy would certainly have been performed in such patients had not irradiation produced a favorable response, and in the second instance because one cannot evaluate to what extent the 2 to 5 month delay in cystectomy necessitated by the preoperative irradiation program permitted an originally resectable lesion to progress to a nonresectable stage.* When a sufficiently large clinical experience with various treatment programs has been accumulated, it should be possible to dissect *total* bladder cancer experience, relative to a surgical treatment program and to the present combined treatment program, to permit at least an attempt to answer the obviously pertinent questions that arise from these considerations. For the present discussion, these potentially important selection factors have been disregarded in the attempt to relate this early experience with combined radiation therapy and radical cystectomy to an experience[4] with radical surgery alone,† fully recognizing the potential limitations of such a comparison.

Although many other aspects of this combined irradiation-cystectomy experience will ultimately necessitate analysis, the results to date will be reviewed briefly relative to the following 4 considerations only: (1) the relationship of the initial

---

* Of course, the converse possibility also exists; namely, that preoperative irradiation may have made some originally nonresectable lesions amenable to radical cystectomy.

† An unspecified number of patients subjected to radical surgery in the Whitmore and Marshall series[4] had had some form of radiation therapy to the bladder prior to radical surgery so that their series does not represent a purely "surgical" experience.

Table I

CYSTOSCOPIC EVALUATION OF RESPONSE TO IRRADIATION

Stage	Uneval-uated	Response		
		Good	Fair	Poor
O, A, B1 (21)	11		2	8
B2, C (26)	9	5	1	11
D1 (3)	2			1
Total	22	5	3	20

clinical stage of the tumor to the cystoscopically judged radiation response; (2) the incidence and nature of the postoperative complications and deaths; (3) the relationship between the initial clinical stage and the postirradiation, post cystectomy pathologic stage of the neoplasm; and (4) an analysis of 2 year survival experience.

RESULTS AND DISCUSSION

In the 4 year interval, 1959 through 1962, a total of 50 patients received preoperative irradiation in anticipation of surgery *and* were subsequently subjected to radical cystectomy in either the Memorial or James Ewing Hospitals. Of this group of 50 patients, 36 received irradiation with cobalt 60, 11 with 1 mev., 2 with the betatron, and 1 with 2 mev. Relative to total dosage to the bladder, 42 patients received approximately 4,000 rads, 4 received approximately 5,000 rads, 1 received 6,000 rads, and 3 received less than 3,000 rads. Although protraction was sometimes made necessary by gastrointestinal effects or by radiation cystitis, the 3 patients who received less than 3,000 rads were the only ones in whom the initially planned dosage of radiation could not be administered. In the latter patients, treatment had to be terminated, in 1 because of gastrointestinal disturbance, in 1 because of the development of urethral obstruction due to tumor, and in 1 because uncontrollable hematuria demanded immediate surgery. Tissue doses of 4,000 rads were generally delivered in 4 to 6 weeks, longer protraction being required only occasionally. Although radiation proctitis and cystitis were the rule, such usually subsided within the month following completion of radiation therapy and, indeed, some patients were entirely asymptomatic at the time of surgery. Treatment was commonly delivered through anterior and posterior portals of a size suitable for encompassing the true pelvis. Complete rotation was used occasionally and a single anterior with two posterior oblique portals only rarely. No serious complications developed during treatment.

I. RELATION OF CLINICAL STAGE OF THE TUMOR TO THE RESPONSE TO IRRADIATION AS JUDGED CYSTOSCOPICALLY

To derive the information shown in Table I, the preradiation cystoscopic findings were compared to the precystectomy cystoscopic findings. The interval between the completion of radiation therapy and the precystectomy cystoscopic examination generally ranged from 1 to 3 months. An unfortunately large proportion of the 50 cases, 22, are listed as "unevaluated." This signifies either that cystoscopic evaluation was not carried out following irradiation or that the cystoscopic findings were not sufficiently definitive to enable the reviewer to render a judgment on the question of radiation response. In the remaining 28 cases, it was possible to make some assessment of response according to the following scale: (a) a good response was one in which marked interval regression or complete disappearance of tumor or tumors was noted; (b) a fair response was one in which some interval regression occurred, but short of a good response; and (c) a poor response was one in which either no definite decrease, or an actual increase, in tumor occurred.

Obviously, subjective factors enter into this type of evaluation but the appraisals were made as objectively as possible. Only 8 of the 28 evaluated patients showed cystoscopic evidence of response to irradiation. Among 10 patients with low stage tumors, no good responses were obtained and only 2 fair responses. Among 18 patients with high stage tumors, 5 good responses were noted and 1 fair response.

Although the numbers are small, the apparent good responses all occurred among patients with deeply infiltrating tumors.

II. POSTOPERATIVE DEATHS AND COMPLICATIONS

An important consideration in evaluating preoperative irradiation is its influence upon the mortality rate and the complication rate following radical cystectomy. In Table II mortality and complication rates following radical surgery[3] alone are compared with those in the present small series of patients in whom preoperative irradiation was followed by radical cystectomy. A postoperative death in the present series was any death occurring in the hospital prior to discharge following radical cystectomy. No major differences are apparent in the mortality rates for the two series. Furthermore, in tabulating the causes of death in the present series (Table III) and comparing this list with the deaths reported following radical surgery alone, the principal and contributory causes of death in the present series are not notably different from those reported in the series of patients having surgery alone. More specifically, it does not seem possible to implicate the preoperative irradiation as a contributory factor in any of the deaths which occurred postoperatively in the present series.

A postoperative complication was defined as an unfavorable occurrence constituting a deviation from an expectedly smooth and favorable course in the hospital following operation. Obviously the reviewer's clinical judgment helps to determine what is and what is not a complication. Inspection of the results in Table II suggests that complications were somewhat more frequent in patients having preoperative irradiation and cystectomy than in those having cystectomy alone. The tabulated experience (Table IV) lists the complications in 31 patients. An analysis of this experience compared with a similar analysis of complications following radical surgery alone indicates that complications such as cardiovascular problems, thrombophlebitis, pneumonia, pyelonephritis, gastrointestinal fistulae, urinary fistulae and intestinal obstruction were probably neither more nor less frequent in the present series than in patients subjected to surgery alone. It has been an impression, however, apparently supported by the relatively high observed incidence of vesical space infections, that such infections are more common in patients who have had preoperative irradiation.

Table II

COMPLICATIONS AND DEATHS

	Radical Cystectomy	Preoperative Irradiation and Radical Cystectomy
Deaths	32/230 (14%)	8/50 (16%)
Complications	116/230 (51%)	31/50 (62%)
No Complications	82/230 (35%)	11/50 (22%)

If one excludes from the morbidity calculations, the 15 patients in whom wound infection, or osteomyelitis of the pubis, or vesical space infection occurred either alone or only in combination with one another, the resultant complication rate becomes 32 per cent (16/50), a rate comparable to that obtained for the surgical series when wound infections and pelvic abscesses are excluded from the morbidity calculations.* One may tentatively conclude that except for an increase in pelvic wound morbidity, preoperative irradiation does not seem to have unfavorably altered either the mortality rate or the complication rate following radical cystectomy.†

III. RELATIONSHIP BETWEEN INITIAL CLINICAL STAGE AND POSTIRRADIATION-POSTCYSTECTOMY PATHOLOGIC STAGE

This relationship is shown in Table V. In the surgical series[3] the difference between the preoperative clinically estimated stage of the tumor and the postoperative pathologically determined stage of the tumor is a consequence only of the clinician's error in estimation. In this combined therapy experience any observed difference may be a consequence not only of the clinician's error in judgment, but also of the effects of the radiation and possibly of the time interval between the initial evaluation and subsequent radical cystectomy. Obviously, it will require a considerably larger experience than that thus far accumulated before any evaluation of the relative importance of these possibilities can be made. In 21 patients in whom the tumor was clinically judged to be only superficially infiltrating, there were only 4 in which deeply infiltrating tumor was found, a clinical accuracy of 81 per cent. In the 29 tumors judged clinically to be deeply infiltrating or metastatic, there were 11 instances in which, at most, superficially infiltrating neoplasm was found, a clinical accuracy of 62 per cent. The over-all accuracy of clinical staging in this group of 50 patients was thus 70 per cent (35/50). In a surgical series of 229 cases,[3] a comparison of the preoperative estimate of the stage of the tumor to the pathologic stage determined by examination of the surgical specimen after radical surgery established an over-all accuracy of 80 per cent (183/229)—75 per cent (48/64) in tumors judged clinically to be of superficially infiltrating stage, and 82 per cent

---

* See Table V in Reference 3. If the 46 instances of wound infection and pelvic abscess are subtracted from the total of 116 patients with complications (not entirely accurate since wound infection may well have occurred concomitant with another complication in some patients), 70 patients (at least) would have remained for a complication rate of 30 per cent (70/230).

† In the radical surgery series of Reference 3, 67 of the 230 patients had pelvic exenteration, an operation with a distinctly higher morbidity and mortality rate than radical cystectomy *per se*. This fact creates a bias which tends to make the mortality and morbidity rates following the combined program seem more favorable than they may actually be.

TABLE III

DEATHS

Case No.	Principal Cause	Contributory Cause(s)	Postoperative Days	Comment
14-39-62	? Cardiorespiratory		6	Autopsy revealed no anatomic cause for death
23-45-74	Electrolyte imbalance	Biliary, ileal and gastric fistulae	59	Gastrostomy and common duct exploration performed at time of anterior exenteration
23-44-56	Gas gangrene		3	Fulminant infection presumably originating around ileal stoma and involving abdominal wall
20-63-76	? Pulmonary embolus	Prolonged ileus; upper gastrointestinal bleeding	26	No autopsy
21-10-40	Peritonitis	Intestinal obstruction	14	Developed peritonitis following laparotomy for intestinal obstruction secondary to adhesions
25-68-38	Chronic sepsis	Pyelonephritis; partial intestinal obstruction	140	Autopsy revealed pelvic recurrence, bilateral severe pyelonephritis
25-75-29	Electrolyte imbalance	Ileal fistula	68	Small bowel fistula developed at ileoileostomy site. Died 1 day after 3rd attempt at repair. Autopsy revealed no anatomic cause for death
24-16-90	Electrolyte imbalance	Pyelonephritis	77	Severe renal damage secondary to obstruction at onset necessitated preliminary bilateral nephrostomy. Ureterosigmoidostomy was the definitive method of diversion

(135/165) in tumors judged clinically to be of deeply infiltrating or metastatic stage. The fact that the over-all accuracy of clinical staging was apparently greater in the surgical series than in the present series implies that either clinical judgment was more frequently in error in this series, or radiation therapy favorably altered the stage of the tumor, or both. The possibility that radiation therapy may have altered favorably the stage of the tumor derives some support from the fact that among the 26 patients with tumors judged clinically to be deeply infiltrating, pathologic examination of the cystectomy specimen revealed *in situ* cancer only in 2 and no residual tumor in 5. Furthermore, among 21 patients with initially low stage tumors (O, A, B1), pathologic examination of the surgical specimen revealed no tumor in 4 instances and *in situ* cancer only in 6. Thus, 17 of 50 patients with initially infiltrating lesions had an apparent reduction in the stage of the bladder tumor as a consequence of radiation therapy.

It is of note that although cystoscopic evidences of radiation effect on neoplasms were more striking in patients with lesions judged clinically to be deeply infiltrating than in patients with superficially infiltrating tumors, the pathologic findings demonstrated favorable effects from radiation therapy both in the superficially infiltrating and the deeply infiltrating lesions. This apparent inconsistency may be an artefact created by the large proportion of "unevaluated" cases shown in Table I.

Table IV

COMPLICATIONS IN 31 PATIENTS

Cardiac Failure	2
Thrombophlebitis	3
Pneumonia	2
Upper Gastrointestinal Bleeding	2
Intestinal Obstruction	2
Staphylococcal Enteritis	1
Gastrointestinal Fistula	3
Ileus	2
Urinary Fistula	1
Pyelonephritis	2
Electrolyte Imbalance	1
Hemorrhage from Site of Surgery	2
Pelvic (vesical space) Infection	20
Wound Infection	4
Osteomyelitis of Pubis	2
Wound Dehiscence	3

Table V

PATHOLOGIC EVALUATION OF RESPONSE TO IRRADIATION

Clinical Stage	Pathologic Stage				
	O, A, B1	B2, C	D1	*In Situ* Cancer	No Tumor Found
O, A, B1, (21)	7	2	2	6	4
B2, C (26)	3	10	6	2	5
D1 (3)	1		2		
All Stages (50)	11	12	10	8	9

It is also of interest in this tabulation that *in situ* cancer persisted even when infiltrating cancer disappeared, lending some support to our impression that *in situ* carcinoma of the bladder responds poorly to radiation. The more frequent occurrence of residual *in situ* cancer in patients with superficially infiltrating tumors than in those with deeply infiltrating tumors is in all probability a reflection of the fact that the majority of patients in whom this combined therapeutic program was recommended for superficially infiltrating tumors had multiple or rapidly recurring lesions, a clinical setting in which multifocal *in situ* cancers might be expected to be more frequent.

One further observation from these data which merits mention at this time is the fact that the radiation therapy employed (usually the relatively modest dose of 4,000 rads in 4 to 6 weeks) had a striking effect on a substantial number of patients with bladder tumors within 1 to 3 months following the completion of the radiation therapy. Of the 50 patients included in this study, no less than 9 had no evidence of tumor and an additional 8 had *in situ* carcinoma only in the pathologic specimen.

IV. TWO YEAR SURVIVAL

In Table VI the 2 year survival experi-

TABLE VI

TWO YEAR SURVIVAL FOLLOWING TREATMENT OF BLADDER CANCER*

Clinical Stage	Radical Cystectomy	Preoperative Irradiation and Radical Cystectomy
O, A, B1	38/68 (56%)	5/10 (50%)
B2, C	46/140 (33%)	6/16 (37%)
D	1/20	0/1

* Numerator = 2 year survivors.
Denominator = total cases.

ence in 27 patients who completed preoperative irradiation and cystectomy prior to December 31, 1960 is analyzed relative to the clinically estimated pretreatment tumor stage and compared to corresponding data from the surgical series.[3] In the latter group of 230 patients, it was necessary to recalculate the survival experience on the basis of the precystectomy *clinical* estimate of tumor stage[4] in order to make the data of the two series more comparable. No significant differences in survival between these two groups of cases are apparent.

CONCLUSIONS

Before attempting any conclusions, the small, recent and selected nature of this series requires emphasis. As tentative conclusions one may suggest the following:

1. Preoperative irradiation followed by radical cystectomy has not produced any definite increase in the surgical mortality over that associated with radical surgery alone.
2. Complications following the combined program have not been notably different from those in the surgical series except for a probable increase in the incidence of important vesical space infection in those receiving preoperative irradiation.
3. As judged by cystoscopic examination alone, the response of deeply infiltrating tumors to radiation therapy seems to be more frequently grossly favorable than the response of superficially infiltrating lesions.
4. As judged by a comparison of the clinical stage of the tumor prior to therapy and the pathologic stage of the tumor determined by examination of the surgical specimen, both superficially and deeply infiltrating tumors may respond favorably to irradiation. Furthermore, approximately one-third of the patients demonstrate pathologic evidence of a reduction in tumor stage following radiation therapy.
5. The persistence of *in situ* carcinoma even after apparent eradication of infiltrating cancer suggests that such lesions are less radiosensitive than infiltrating ones.
6. No apparent difference in 2 year survival has been demonstrated in patients treated by radical surgery alone, or by preoperative irradiation and radical surgery.
7. The difficulties of assembling entirely comparable groups of patients treated on the one hand by radical surgery and on the other by preoperative irradiation and radical surgery are evident in this study.

Willet F. Whitmore, Jr.
Urologic Service of the Department of
Surgery
Memorial Hospital
New York, New York

REFERENCES

1. JEWETT, H. J., and STRONG, G. H. Infiltrating carcinoma of bladder; relation of depth of penetration of bladder wall to incidence of local extension and metastases. *J. Urol.*, 1946, *55*, 366–372.
2. MARSHALL, V. F. Relation of preoperative estimate to pathologic demonstration of extent of vesical neoplasms. *J. Urol.*, 1952, *68*, 714–723.
3. WHITMORE, W. F., JR., and MARSHALL, V. F. Radical total cystectomy for cancer of bladder; 230 consecutive cases five years later. *J. Urol.*, 1962, *87*, 853–868.
4. WHITMORE, W. F., JR., and MARSHALL, V. F. Unpublished data.

VOL. 90, No. 5

COMBINED THERAPY, IRRADIATION AND SURGERY, FOR ADVANCED CANCER OF THE LARYNGOPHARYNX*

By SIDNEY M. SILVERSTONE, M.D.,† JOSEPH L. GOLDMAN, M.D.,‡
and HENRY D. ROSIN, M.D.§
NEW YORK, NEW YORK

IN OUR previous publications on the management and survival rate of patients with cancer of the larynx and laryngopharynx, we indicated that the prognosis is dependent upon location as well as on the extent of the neoplasm and that our results of treatment with radiation were comparable to those reported with surgery. A comparative summary of these results is shown in Table I with a classification that has been found clinically useful.

The neoplasms limited to the intrinsic larynx offer the best prognosis. If the growth is confined to one vocal cord, equally high cure rates are obtained with either radiation therapy or partial laryngectomy, but the voice is preserved better with radiation therapy. In more extensive involvement of the intrinsic larynx, the cure rates with either radiation therapy or laryngectomy are again comparable, but radiation therapy has the particular advantage of preserving the larynx. Furthermore, laryngectomy may be successfully performed in the radiation failures, thereby increasing the total over-all cure rate.

With the neoplasms of the extrinsic larynx, or the laryngopharynx, the cure rates with either modality are distinctly lower, particularly so if the posterolateral structures are involved either as the site of origin or by extension from the glottic or supraglottic regions. The extrinsic lesions are usually much larger than the intrinsic and infiltrate the surrounding tissues and structures more widely and more frequently and there is also a much higher incidence of cervical lymph node metastases.

CAUSES OF FAILURE

The predominant cause of failure with either method of management is local recurrence of the neoplasm or uncontrolled lymph node metastases rather than distant metastases. In some cases, the local recurrence can be successfully controlled by further surgical or radiotherapeutic procedures. However, the high incidence of failure to eradicate the disease locally is indicative of the inadequacy of either surgery or radiation therapy as the primary method of management for advanced cancer of the laryngopharynx. Neither method by itself is radical enough, even though each method has been utilized to its fullest capacity. Higher dosage with radiation therapy can result only in adverse complications, while radical surgery has approached the maximum limit of excisability of vital anatomic structures. In all probability, both surgery and radiation therapy have reached the peak of their technical efficacy and no significant improvement in either modality is anticipated at the present time.

Although the radical surgical procedure is carried through normal tissues that are beyond the visible tumor, the recurrences which appear later at the operative site can only be explained as having developed from minute foci of cancer cells that were left *in situ* at the time of surgery. Either they were there originally in the deep fascial planes or lymphatic vessels, or they were liberated and implanted there by the unavoidable manipulation of the tumor mass during its surgical removal. This limitation of the radical operation cannot be overcome by any modification of the surgical procedure.

---

* From the Departments of Radiotherapy and Otolaryngology, The Mount Sinai Hospital, New York, New York.
Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963. Part of Symposium: Preoperative Irradiation; Chairman, Dr. Milton Friedman, New York, New York.

† Attending Radiotherapist, The Mount Sinai Hospital, New York, New York.

‡ Director of Department of Otolaryngology, The Mount Sinai Hospital, New York, New York.

§ Chief Resident, Department of Otolaryngology, The Mount Sinai Hospital, New York, New York; and U. S. Public Health Service Trainee, National Institute of Neurological Diseases and Blindness, U. S. Public Health Service.

At the completion of radiation therapy, the tumor frequently disappears while the laryngopharynx is often restored to its normal status. However, after an unpredictable interval, weeks or months or years, at a time when there may be evidence of late radiation effects, local recurrence of the growth may also develop, most often in the same region as the original neoplasm. Therefore, while radiation therapy apparently destroyed the peripheral areas of the neoplasm, it effected only temporary restraint of the growth in the region of its site of origin. Evidently the peripheral areas of the neoplasm, including the numerous small foci of cancer cells which are present interstitially or in lymphatic vessels, often have a greater degree of radiosensitivity and are therefore more easily destroyed. This differential radiation effect corresponds to the frequent observation during the course of treatment by radiation that the peripheral areas of the neoplasm are the first to disappear whereas the tumor at the site of origin disappears last, or, instead, persists as a residuum. When the tumor cells recover from the mitotic inhibitory effect of the radiation, the newly produced cancer cells have the activity and growth potential of the original neoplasm. The recurrent growth consists of new generations of cancer cells unaffected by the previous radiation therapy. Therefore, clinically, the patient has regressed to the poor prognostic status he originally had before treatment. This limitation of radiation therapy due to differential radiosensitivity cannot yet be overcome by any modification of radiation techniques, although experimental studies with oxygenation and chemotherapy may possibly reveal new methods of increasing neoplastic radiosensitivity.

RATIONALE OF COMBINED THERAPY

Radical surgery would offer a better prognosis for advanced cancer of the laryngopharynx if the original extent of the tumor involvement could be appreciably

TABLE I

CANCER OF LARYNX AND LARYNGOPHARYNX 5 YEAR SURVIVAL RATES

	Radiation Therapy Per Cent		Surgery Per Cent	
	Determinate	Absolute	Determinate	Absolute
Intrinsic Larynx				
Vocal Cord Lesions: early (suitable for partial laryngectomy)	88	70	83	59
Advanced Lesions (would require total laryngectomy)	63	49	66	55
Extrinsic Larynx (laryngopharynx)				
Anterior Group: supraglottic (limited to false cord and laryngeal surface of epiglottis)	56	47	58	—
Posterolateral Group: hypopharynx (involvement of aryepiglottic fold, arytenoid, pyriform sinus, postcricoid)	24	19	22	—

reduced so that the operation can be performed truly wide of the limits of the neoplasm. It would then be the equivalent of an operation for an early lesion instead of an advanced one. Radiation therapy would also be significantly more successful if the undestroyed but clinically quiescent residuum of disease was removed before it could resume its growth activity.

Therefore, radiation therapy and surgery can be combined to provide a superior method of management if they are correctly timed for their maximum beneficial effects. Radiation is administered first to reduce the tumor mass and to destroy its peripheral infiltrative extensions so that the surgery which follows can be truly radical. It is essential, however, that the surgery be performed early before there is recovery of growth activity of the residuum, as otherwise the value of preoperative irradiation would be lost. It is upon this reasoning that our plan of combined therapy has been formulated. Combined therapy is not the same as surgery for a recurrence after radiation therapy. Combined therapy is an integrated program of radiation therapy followed by radical surgery at a specified interval, and the surgery must be performed even if clinically there appears to be no evidence of disease after the irradiation is completed. This paper is a report to show not only that combined therapy is technically feasible but also that the early results are highly encouraging.

COMBINED THERAPY

The plan of combined therapy comprises three phases: cobalt 60 teletherapy for a tumor dose of 5,500 rads in 5 weeks, a rest interval of 3 to 6 weeks, and then radical surgery.

COBALT 60 TELETHERAPY

The required dose of radiation must be adequate to destroy completely the peripheral extensions of the neoplasm but within the limits of tolerance of the normal tissues so as not to compromise the surgery which follows later. On the basis of our previous radiotherapeutic experience and our early cases in this study, a tumor dose of 5,500 rads in 5 weeks was considered to be the most favorable to accomplish this objective. For a dose of this magnitude, however, radiation in the quality range of cobalt 60, supervoltage, or megavoltage is required in order to spare the skin and subcutaneous tissues. Except for our first case, we have employed cobalt 60 teletherapy for this purpose.

The gamma radiation of cobalt 60 is directed to the entire laryngopharynx, or beyond, to encompass the tumor-bearing structures including the palpable cervical lymph nodes. This is accomplished through parallel opposing lateral cervical fields which are often necessarily large, from 6×8 cm. to as much as 10×12 cm. The tissue structures encompassed by the beam of radiation are checked for each field by appropriate roentgenograms. If the irradiated volume must include the spinal cord, adjustments are made so that the spinal cord itself does not receive a dose in excess of 3,500 rads in order to avoid the risk of radiation myelitis.

Radiation therapy is usually well tolerated and can therefore be administered on an ambulatory basis. The mucosal reactions consist of congestion and patchy membrane formation. The chief complaints are dryness and loss of taste. The skin shows mild to moderate erythema followed by pigmentation and dry desquamation but never moist desquamation. The subcutaneous tissues remain soft and supple.

THE REST INTERVAL

About 3 weeks after completion of radiation therapy, the tumor is either no longer visible or reduced to a minimum, and, except for occasional slight edema, the radiation reactions subside and the laryngopharyngeal structures return to an almost normal appearance. A favorable effect is also observed in the involved lymph nodes. Some lymph nodes disappear completely. Others are reduced in size. Fixed lymph nodes frequently become movable. Occa-

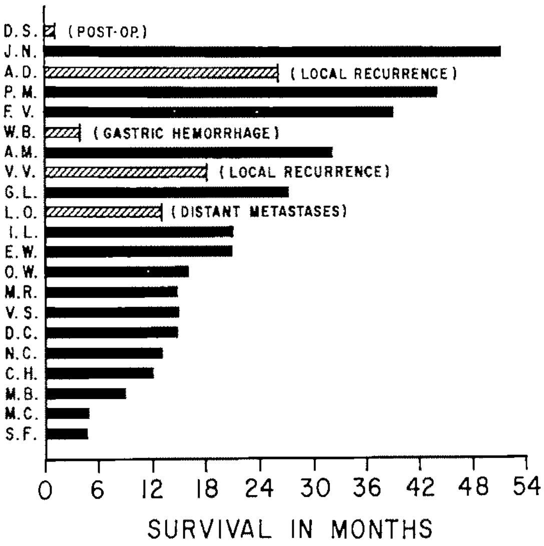


Fig. 1. Clinical Results. Of 21 patients treated, 16 (solid bars) were living and well at 5 to 51 months, without evidence of disease.

sionally a large mass of lymph nodes becomes cystic because of necrosis and liquefaction.

At this phase, the laryngopharynx and the neck are in the best physiologic state that they ever will be for that particular patient. The extent of the neoplasm has been greatly reduced and there is no fibrosis or endarteritis of the normal tissues. This is the most favorable time for the surgery, because after a longer interval the late radiation changes occur together with a high probability of recurrence of the neoplasm. Since the length of this biologically favorable period is unknown, we prefer to perform the surgery early, between the third and the sixth week after the radiation therapy is completed. The longer the delay beyond that period, the greater is the risk of recurrence.

SURGERY

The operation to be performed is the same radical surgical procedure that would have been done originally if surgery would have been the primary method of treatment. In general, it consists of wide field laryngectomy together with neck dissection on one or both sides as indicated by the clinical status.

ANALYSIS OF CASES

EXTENT OF NEOPLASM

To date, 21 patients with advanced cancer of the laryngopharynx have completed combined therapy. Each case was classified as Stage III, according to the rules of the Clinical Stage Classification of Malignant Tumors of the Larynx presented at the Seventh International Congress of Cancer in London, 1958. A detailed extent of the primary neoplasm and the palpable cervical lymph nodes is shown for each case in Table II. In 4 cases, the neoplasm obstructed the airway severely enough to require tracheostomy as an emergency procedure, in 3 cases before radiation therapy was begun and in 1 shortly after treatment was started.

In every case, biopsy was performed and reported as squamous cell carcinoma. In only a few cases, however, was biopsy of the palpable lymph nodes obtained. In most of the cases, biopsy of the lymph nodes was not done and their evaluation was therefore clinical.

In all cases, the clinical evaluation of the extent of the primary tumor was supported by roentgenographic studies of the larynx and neck, including frontal and lateral views and laminagraphy. In some of the more recent cases, laryngography has been added.

MANAGEMENT AND SURVIVAL

Except for several cases at the beginning of our study, the dose of radiation has been 5,500 rads in 5 weeks and the average post-radiation rest interval before surgery was 5 weeks. Thus, radical surgery was performed at approximately 10 weeks from the onset of therapy. In 4 of the cases, radical neck dissection was required on both sides. In 1 case, both sides were done at the same time; in the other 3, the second side was done at intervals of 3, 4, and 8 weeks after the initial radical procedure.

Of the 21 patients treated, there are 16 who are living and well with no evidence of disease from 5 to 51 months (Fig. 1). All of them have become adjusted to their disability and some of them have mastered an esophageal voice. All patients are being observed at regular intervals at our follow-up clinic.

Of the 5 cases which died, there was only 1 postoperative death (D.S.) due to myocardial infarction on the 13th day. Of special interest in this patient is that, during the performance of emergency tracheostomy, a minute metastatic lymph node was found just anterior to the trachea. It was the opinion of the surgeon that if subsequently only a neck dissection had been done without laryngectomy, this minute metastatic focus might have been overlooked because of its location. The second death occurred from a gastric hemorrhage, 4 months after the onset of therapy, in a case (W.B.) with a known ulcer history. Postmortem examination showed no evidence of recurrence in the neck. A third case (A.D.) died of cancer after 2 years and 2 months. Because no lymph nodes were palpable in an elderly male (75 years), the operative procedure was limited to laryngectomy. However, the subsequent appearance of metastatic cervical lymph nodes required bilateral neck dissection which proved inadequate to control the rapid advance of the growth to which the patient succumbed. This case illustrated the need for the radical procedure at the original operation. A fourth case (V.V.) died of local recurrence in the tongue after 1 year and 6 months. A review of the details of treatment revealed that the irradiated volume should have included more of the pre-epiglottic space and tongue for a lesion in which the vallecula and base of tongue are involved and, similarly, the surgery should have been more extensive. Subsequent radiation therapy directed to the recurrence effected only temporary remission. In the fifth case (L.O.), the primary neoplasm and cervical metastases responded well to combined therapy but 1 year later the patient succumbed to pulmonary metastases superimposed upon pulmonary tuberculosis.

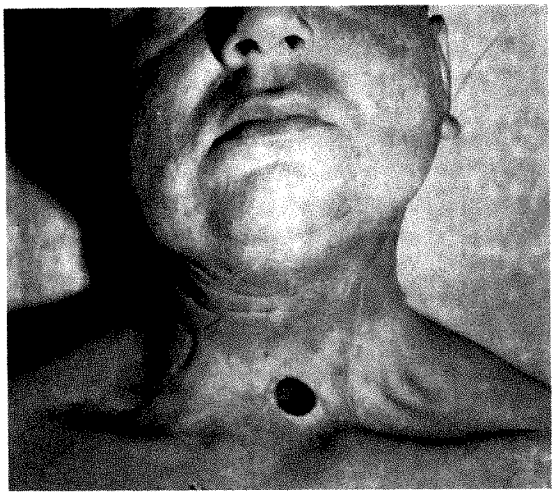


FIG. 2. Case D.C., 5 months after completion of combined therapy which included bilateral neck dissection. Excellent healing of skin, minimal induration of subcutaneous tissues.

COMPLICATIONS

The initial uncertainty with combined therapy was whether or not the irradiated tissues would heal after radical surgery. It was also thought that the surgery might be made more difficult by increased vascularity, edema, or fibrosis. However, none of these difficulties were encountered (Fig. 2) probably because of the timing of the surgery before the late radiation changes became manifest.

Fistula formation occurred in 8 cases but all of them healed completely and no fistula lasted more than 6 weeks. Wound infections also occurred but healing was effected in every instance. Most of the complications occurred in the early cases of this series, and in the last 7 cases treated there has been only 1 fistula.

Because irradiated tissues heal more slowly and are more vulnerable to trauma, the surgical technique has been modified to ensure sterility and to eliminate trauma. A nasogastric tube is passed preoperatively.

Table II

Case	Local Clinical Status	Lymph Nodes	Classification
D.S. 53 F	Right pyriform sinus, arytenoid, aryepiglottic fold, base of epiglottis; right larynx *fixed;* tracheostomy during radiation therapy	Right subdigastric; *fixed*	Stage III T-4, N-2
J.N. 68 M	Right and left vocal cords, ventricles, false cords, anterior commissure, right arytenoid, subglottis; right cord *fixed;* tracheostomy before radiation therapy	Right mid-jugular	Stage III T-3, N-1
A.D. 75 M	Right and left vocal cords, anterior commissure, right ventricle, false cords, arytenoid, aryepiglottic fold; right vocal cord *fixed*	None	Stage III T-3, N-0
P.M. 58 M	Right aryepiglottic fold, epiglottis, vallecula, base of tongue	None	Stage III T-4, N-0
F.V. 35 M	Left aryepiglottic fold, arytenoid, pyriform sinus, vocal cord, ventricle, false cord, epiglottis	Left mid-jugular; *fixed*	Stage III T-4, N-2
W.B. 67 M	Right subglottis, vocal cord *fixed,* arytenoid, aryepiglottic fold; tracheostomy before radiation therapy	Right mid-jugular	Stage III T-3, N-1
A.M. 50 M	Left vocal cord *fixed,* ventricle, false cord, arytenoid, aryepiglottic fold, epiglottis, vallecula	Left upper jugular	Stage III T-4, N-1
V.V. 55 M	Epiglottis, vallecula, base of tongue	Bilateral; extensive	Stage III T-4, N-2
G.L. 36 M	Right and left aryepiglottic folds, epiglottis, vallecula, base of tongue	Left upper jugular	Stage III T-4, N-1
L.O. 61 M	Right vocal cord *fixed,* ventricle, false cord, subglottis, aryepiglottic fold, arytenoid, pyriform sinus	Right upper and mid-jugular; *fixed*	Stage III T-4, N-2
I.L. 43 F	Right pyriform sinus, arytenoid, aryepiglottic fold, epiglottis, lateral pharyngeal wall; right larynx *fixed*	Right upper and mid-jugular	Stage III T-4, N-1
E.W. 57 M	Epiglottis, vallecula, base of tongue, pre-epiglottic space, right lateral pharyngeal wall	Bilateral upper jugular, subdigastric	Stage III T-4, N-2
O.W. 54 M	Right and left vocal cords, right vocal cord *fixed,* anterior commissure, base of epiglottis, right ventricle, false cords, subglottis, arytenoid; tracheostomy before radiation therapy	Right mid-jugular	Stage III T-3, N-1
M.R. 70 M	Right vocal cord *fixed,* ventricle, false cord, arytenoid	Right upper jugular	Stage III T-3, N-1
V.S. 61 F	Right pyriform sinus, lateral wall	Right mid-jugular	Stage III T-4, N-1
D.C. 38 M	Epiglottis, anterior commissure, right and left false cords, inter-arytenoid area, limited mobility of right vocal cord	Bilateral mid-jugular, right supraclavicular	Stage III T-3, N-2
N.C. 56 M	Left aryepiglottic fold, pyriform sinus, arytenoid, epiglottis	None	Stage III T-4, N-0

Table II (*Continued*)

Case	Local Clinical Status	Lymph Nodes	Classification
M.B. 49 F	Left aryepiglottic fold, arytenoid, *fixed* vocal cord, ventricle, false cord	Left subdigastric	Stage III T-3, N-1
C.H. 60 M	Right and left arytenoids, right pyriform sinus, aryepiglottic fold, epiglottis, vallecula, base of tongue; right larynx *fixed*	Right multiple; extensive	Stage III T-4, N-1
M.C. 52 M	Left pyriform sinus, lateral pharyngeal wall, aryepiglottic fold, false cord, epiglottis; vocal cord *fixed*	Left upper jugular	Stage III T-4, N-1
S.F. 62 M	Right vocal cord *fixed*, ventricle, false cord, anterior commissure, epiglottis, arytenoid	Right mid-jugular	Stage III T-3, N-1

Closure of the pharynx is effected by multilayered interrupted sutures instead of continuous suture. The method of drainage has been modified to eliminate tissue trauma caused by heavy rubber suction tubes. Postoperative care is a meticulous procedure to avoid infection or trauma.

The successful surgical experience with complete wound healing in every case indicates that combined therapy is technically feasible.

CLINICAL AND PATHOLOGIC CORRELATION

It is interesting to note that in 13 of the 21 cases, laryngeal examination after radiation therapy and just before surgery revealed no definite evidence of disease while in the remaining 8 there was considerable reduction of the tumor mass. Only the first 10 cases were studied histologically in the routine way and 4, which were clinically negative, also showed no histologic evidence of disease. However, another case which was clinically negative did show a submucosal focus of residual carcinoma in the pyriform sinus (Fig. 3). Because of this finding a new investigation has been undertaken in which the entire surgical specimen comprising the larynx is fixed as a unit for whole larynx sections. Therefore, beginning with our 11th case, all surgical specimens are submitted to this special study, the results of which will be reported at a future date when completed.

Palpable cervical lymph nodes were noted in 18 of the 21 cases, and in 8, residual carcinoma was found histologically after combined therapy. In some cases, the metastatic lymph nodes may have been destroyed by the radiation. However, since many lymph nodes may be missed if the pathologic examination is done in the ordinary routine way, all neck dissection specimens are now being subjected to serial sectioning. Therefore, the final evaluation of the histologic status of the lymph nodes in all cases will be delayed until this project is completed.

There were 14 cases with fixed vocal cords. After completion of radiation therapy, return of movement was associated with a negative larynx on clinical examination in 11 cases, while in the 3 cases in which fixation persisted there was also residual disease clinically.

DISCUSSION

Our studies indicate that combined therapy is a feasible method of management for advanced cancer of the laryngopharynx. It can be accomplished with minimum morbidity although it requires about 3 months to complete.

The major objection that can be raised is that some normal larynxes may be removed. That this may be true cannot be denied. However, in the absence of any test or method of recognizing the larynx in which all traces of cancer have been destroyed by radiation therapy, it is far safer to proceed with its removal than to risk a recurrence of growth that is most likely to

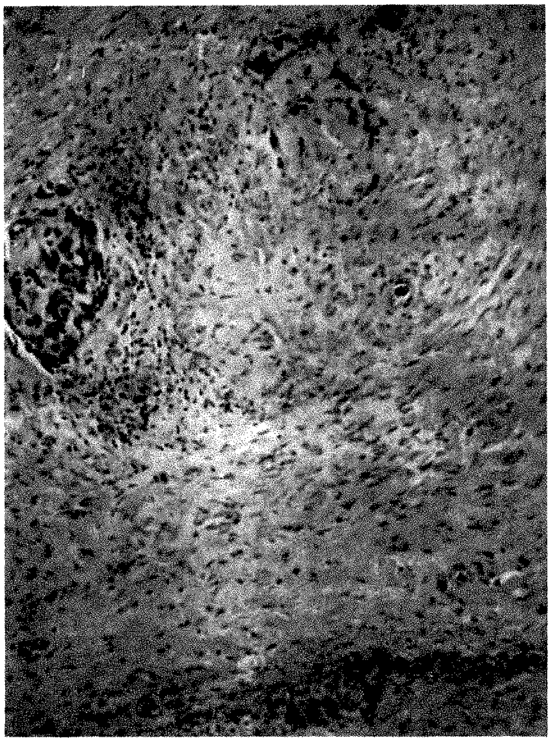


FIG. 3. Case L.O. Photomicrograph showing submucosal focus of carcinoma cells in larynx which clinically appeared normal at time of surgery 4 weeks post radiation.

prove fatal, especially since the recurrence rate for this disease is high. The clinical appearance of the larynx after radiation therapy is too deceptive to be accepted as free of disease. Therefore, because of the known low cure rate for advanced cancer of the laryngopharynx by radiation therapy alone and also because the larynx would have been removed in any case if surgery alone were the treatment of choice, there should be no objection to the removal of a possibly normal larynx if combined therapy should prove to be the superior method of management that our present studies indicate it to be.

SUMMARY AND CONCLUSIONS

1. The cure rate for advanced cancer of the laryngopharynx is poor, in the order of about 20 per cent or less with either radiation therapy or surgery.

2. Local recurrence is the predominant cause of failure with either method. With surgery, it arises from cancer foci in the operative site. With irradiation, it arises from the residuum after the destruction of the peripheral extensions of the growth.

3. Combined therapy encompasses the advantageous effects of both modalities: irradiation to eliminate the peripheral extensions of the growth, followed, after a limited rest interval, by radical surgery to eliminate the residuum.

4. A dose of 5,500 rads in 5 weeks with cobalt 60 teletherapy effects adequate tumor regression without compromising the normal tissues for the surgery which follows, and is therefore considered most favorable for preoperative radiation therapy.

5. A rest interval of 3 to 6 weeks is chosen because during this period the early radiation reactions have subsided and the late radiation effects have not yet become manifest, while the growth has been reduced to its minimum. Local recurrence generally appears later and is indicative of tumor cell recovery from the growth restraint effect of the radiation.

6. The surgery is as radical as would have been if radiation therapy was not administered preoperatively.

7. Twenty-one cases of advanced cancer of the laryngopharynx, all Stage III, have completed combined therapy and 16 have survived to date from 5 to 51 months. Of the 5 deaths, 2 were due to local recurrences, 1 to distant metastases, and 2 to other causes.

8. No technical difficulties that might be attributed to the irradiation were encountered at operation. Complications of wound infection and fistula formation occurred in 8 cases and all healed completely. Technical modifications have been introduced to eliminate infection and trauma.

9. The larynx and laryngopharynx frequently have a normal appearance after radiation therapy but there may be foci of cancer cells in the submucosa not seen on clinical examination. Favorable effects of

the irradiation are also noted in the lymph node metastases.

10. Our studies demonstrate that combined therapy is a feasible method of management for advanced cancer of the laryngopharynx. The satisfactory results achieved thus far have encouraged us to continue further with this program.

Sidney M. Silverstone, M.D.
945 Fifth Avenue
New York 21, New York

REFERENCES

1. Buschke, F., and Galante, M. Radical preoperative roentgen therapy in primarily inoperable advanced cancers of head and neck. *Radiology*, 1959, *73*, 845–848.
2. Cantril, S. T. Radiation therapy in cancer of larnyx: review. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1959, *81*, 456–474.
3. Cantril, S. T. Radiation therapy in cancer of larynx. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1960, *83*, 17–20.
4. Fletcher, G. H., and Jesse, R. H., Jr. Contribution of supervoltage roentgenotherapy to integration of radiation and surgery in head and neck squamous cell carcinomas. *Cancer*, 1962, *15*, 566–577.
5. Goldman, J. L., and Silverstone, S. M. Role of radiation therapy in carcinoma of larynx. *Ann. Otol., Rhin. & Laryng.*, 1960, *69*, 890–905.
6. Goldman, J. L., and Silverstone, S. M. Combined radiation and surgical therapy for cancer of larynx and laryngopharynx. *Tr. Am. Acad. Ophth.*, 1961, *65*, 496–507.
7. Harris, W., Kramer, R., and Silverstone, S. M. Radiation therapy for cancer of the larynx. In: Clinical Therapeutic Radiology. U. V. Portmann, Editor. Thomas Nelson & Sons, New York, 1950, pp. 136–158.
8. Harris, W., Silverstone, S. M., and Kramer, R. Roentgen therapy for cancer of larynx and laryngopharynx. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1954, *71*, 813–825.
9. Lederman, M. Place of radiotherapy in treatment of cancer of larynx. *Brit. M. J.*, 1961, *1*, 1639–1646.
10. Lederman, M. Carcinoma of laryngopharynx: results of radiotherapy. *J. Laryng. & Otol.*, 1962, *76*, 317–334.
11. Leroux-Robert, J. Étude statistique de 644 cas de cancers du larynx et de l'hypopharynx traités par chirurgie au associations radiochirurgicales. *Ann. oto-laryng.*, 1959, *76*, 533–566.
12. MacComb, W. S. Treatment of head and neck cancer; Janeway Lecture, 1960. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1960, *84*, 589–609.
13. McGavran, M. H., Bauer, W. C., and Ogura, J. H. Incidence of cervical lymph node metastases from epidermoid carcinoma of larynx and their relationship to certain characteristics of primary tumor; study based on clinical and pathological findings for 96 patients treated by primary en bloc laryngectomy and radical neck dissection. *Cancer*, 1961, *14*, 55–66.
14. Roxo-Nobre, M. O. Clinical stage classification of malignant tumors of larynx. *Acta Unio internat. contra cancrum*, 1960, *16*, 1865–1873.
15. Silverstone, S. M., and Simon, N. Advantages of cobalt-60 in practice of radiotherapy. *J. Mt. Sinai Hosp.*, 1957, *24*, 124–136.

HISTOLOGY, NATURAL HISTORY AND RESULTS OF TREATMENT OF MUCOUS GLAND TUMORS*

By MARGARET D. SNELLING, M.R.C.P., F.R.C.S., F.F.R.
LONDON, ENGLAND

MUCOUS gland tumors are among the most interesting growths of the head and neck encountered by radiotherapists and the wide variation in their mode of presentation, life history, spread and histology, together with the difficulties associated with their treatment, combine to make them a challenging problem.

These tumors occur in the major salivary glands and also in the numerous secreting goblet cell glands found throughout the mucosa of buccal and nasal cavities, pharynx and air passages; however, only tumors of the palate, tonsil and peritonsillar region, lateral pharyngeal wall, nasal cavity, nasopharynx and sinuses will be discussed in this paper.

DISTRIBUTION OF CASES

Between the years 1928 and 1962 inclusive, 73 cases of mucous gland tumors were seen (Table I). More than half of these (40) occurred in the palate and another 13 in the maxillary antrum—there is little doubt that some of the latter, in fact, started in the palate and later spread to include the antrum. Tumors were rare in other sites but included 6 cases in the nasopharynx and 4 in the nasal cavity, 4 peritonsillar tumors, 3 in the lateral pharyngeal wall and 3 ethmoid tumors.

The important tumors are those of the mixed parotid type and cylindromas (basaliomas, adenoid cystic carcinomas). There were 40 of the former and 26 of the latter as well as 2 cases of mucoepidermoid tumor and 5 cases of carcinoma (Table II). A number of cases of cylindroma occurring in the floor of the mouth, tongue, lips, cheeks and trachea as well as some cases of mixed parotid tumor have been omitted from this review.

Table I

SITE OF MUCOUS GLAND TUMORS
1928–1962

Palate	40 (54.8%)
Maxillary antrum	13 (17.8%)
Nasopharynx	6
Nasal cavity	4
Peritonsillar region	4
Ethmoids	3
Lateral pharyngeal wall	3
Total	73

MIXED PAROTID TUMOR

These tumors vary greatly in behavior and prognosis. A mixed parotid tumor similar to that occurring in the parotid gland is lobulated and apparently encapsulated, but, although it may seem to be removable by enucleation, late recurrence is common because of extension of the growth through the apparent capsule. Recurrence of this tumor may occur 20 or 30 years after the first removal and it may eventually acquire malignant characteristics and infiltrate or metastasize—for example, 1 of our patients who was treated for a mixed parotid type tumor of the peritonsillar region died 20 years after the original operation with metastases in bone. Because of this liability to recurrence, it is our policy to treat these

Table II

TYPE OF MUCOUS GLAND TUMORS
1928–1962

Mixed parotid type	40 (54.8%)
Cylindroma	26 (35.6%)
Mucoepidermoid tumor	2
Carcinoma	5
Total	73

---

* Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963.

cases by wide excision wherever possible, and, when adequate primary excision is not possible owing to extent or site, to precede the operation by a course of radiation therapy using supervoltage techniques and giving a dose of approximately 5,500 rads over a period of 5 to 6 weeks. The operation is performed 6 weeks after the end of the radiation therapy.

CYLINDROMA

The cylindroma or basalioma is a much more dangerous tumor owing to its tendency to early wide invasion. The tumor consists of columns of epithelial cells enclosed in cylinders of "hyaline tissue;" these cells sometimes undergo mucoid change when large cysts develop and the growth presents a net-like pattern. Although apparently circumscribed, the growth spreads early, especially along the nerve sheaths and a seemingly cured tumor of the palate or antrum may reappear after many years as a tumor in the base of skull. In some cases nerve pain has been the first symptom. In 1 case the diagnosis was made by the neurosurgeon who explored the region of the fifth nerve ganglion because of intractable pain and found an intracranial nodule of tumor. Although these tumors have a very long natural history, the ultimate prognosis is extremely bad except in tumors of the palate, where adequate wide excision is possible. Because of the wide extension, all operations are now preceded by very wide field supervoltage therapy which is continued to the limit of tissue tolerance, usually 6,000 to 7,000 rads over 7 or 8 weeks. The margin around the tumor is considerably larger than that of a mixed parotid tumor and the base of the skull is always included.

MUCOEPIDERMOID TUMORS AND CARCINOMA

These tumors are both rare. The mucoepidermoid tumors are said to have a tendency to local recurrence and surgery is preceded or followed by radiation therapy depending on the site and extent of the tumor. Of 2 cases of mucoepidermoid tumor in this series, 1 recent case occurred in the maxillary antrum; the other patient who had a palatal tumor is well and without recurrence more than 5 years after treatment. The carcinoma arising in the mucous glands appears to be of high degree of malignancy and in all our cases there was early invasion of the lymph nodes. Treatment is by a combination of surgery, including block dissection, with radiation therapy, but, in our 5 cases 4 died of carcinoma within a few years of treatment and the last one died after 16 years following repeated operations on the primary and metastatic disease and several courses of radiation therapy. In these cases there is no doubt that, although cure was not achieved, prolonged survival and increased comfort resulted from repeated treatments.

Table III shows the distribution of the different types of tumors. Over half (40) occurred in the palate and at this site again over half the tumors (25) were of the mixed parotid type. Eleven were cylindromas. There was 1 mucoepidermoid tumor and 3 cases of carcinoma. In the maxillary antrum, of 13 tumors only 2 were of the mixed parotid type and 9 were cylindromas. There may be some inaccuracy here, since from the history it appears that some of the cylindromas and at least 1 of the mixed parotid tumors may have started in the palate. In the ethmoids and nasopharynx there were equal numbers of mixed parotid tumors and cylindromas, but in the nasal cavity, peritonsillar region and lateral pharyngeal wall there was a definite preponderance of mixed parotid tumors.

RESULTS OF TREATMENT

It is difficult to present the results of treatment in conditions where recurrence often occurs 10 or 20 or even more years after the original treatment. The 5 year results give little picture of the disease and Table IV therefore shows only the number of known recurrences, the 5 year survival and any later developments that are known to have occurred. Since a number of these patients have been treated only 5 to 10

Table III

DISTRIBUTION OF MUCOUS GLAND TUMORS
1928–1962

Site	Mixed Parotid Type	Cylindroma	Mucoepidermoid Tumor	Carcinoma	Total
Palate	25	11	1	3	40 (54.8%)
Maxillary antrum	2	9	1	1	13 (17.8%)
Ethmoids	1	1	—	1	3
Nasopharynx	3	3	—	—	6
Nasal cavity	3	1	—	—	4
Peritonsillar region	3	1	—	—	4
Lateral pharyngeal wall	3	—	—	—	3
Total	40 (54.8%)	26 (35.6%)	2	5	73

years ago, it will be appreciated that these figures are by no means final.

The first column in Table IV shows the number of patients seen; after that the figures refer to patients seen, and mostly treated, between the years of 1928 and 1957 inclusive. Treatment obviously varied with the years, starting with surgery and occasionally radium needle implantation and ending with a planned treatment consisting of surgery alone whenever possible in cases of mixed parotid tumors, surgery with radiation therapy in the more extensive or inaccessible cases and always surgery preceded by wide field irradiation in the cases of cylindroma. The radiation therapy has changed from radium needle implantation to planned external deep roentgen therapy and then to external irradiation by supervoltage.

Of 28 cases of mixed parotid tumor seen before 1958, 5 were lost within a few years

Table IV

RESULTS OF TREATMENT OF MUCCUS GLAND TUMORS
1928–1957

	1928–1962	1928–1957					
	Total Seen	Total Seen	No Recurrence	Recurrence	Lost	Five Year Survival	Later Developments
Mixed parotid type	40	28	14	9	5	22 (78.6%)	Died of cancer—2 cases Alive with cancer—3 cases
Cylindroma	26	21 (1 case died postoperatively)	5	14	1	14 (66.6%)	Died of cancer—7 cases Alive with cancer—1 case
Mucoepidermoid tumor	2	1	1			1	
Carcinoma	5	5		5		1	Died of cancer—1 case
Total	73	55	20 (36.4%)	28 (50%)	6	38 (69.1%)	Died of cancer—10 cases Alive with cancer—4 cases

Table V

RESULTS OF TREATMENT OF PALATAL TUMORS
1928–1957

	1928–1962	1928–1957					
	Total Seen	Total Seen	No Recurrence	Recurrence	Lost	Five Year Survival	Later Developments
Mixed parotid type	25	17	10	3	4	13	
Cylindroma	11	9	5	3 Died of cancer—1 case (3 yr.)	1	7	Died of cancer—2 cases
Mucoepidermoid tumor	1	1	1			1	
Carcinoma	3	3		3 Died of cancer—2 cases (2, 3 yr.)		1	Died of cancer—1 case
Total	40	30	16	9	5	22	Died of cancer—3 cases

—mostly during the War—but 1 of these is thought to have recurred. Twenty-two patients, or 78.6 per cent, survived 5 years; of these 2 died of carcinoma, 7 and 20 years after the original treatment and 3 are alive with carcinoma, 1 at 9 and 2 at 15 years after the first treatment. One of the deaths was due to metastases, the other to invasion of the base of the skull. Of the remaining 17 five year survivals, 5 have had recurrences treated and are apparently without disease, the other 12 patients have had no recurrences.

Of 21 patients with cylindroma, 1 died from hemorrhage after an operation, 1 is lost and 14 have had recurrences. Fourteen cases survived 5 years but of these 7 later died with carcinoma after intervals of from 5 to 13 years after the first treatment and 1 is alive with pulmonary metastases at 10 years. Only 6 of the 21 cases are therefore apparently without disease; in 5 of these the cylindroma occurred in the palate, the other is a young woman with extensive disease in the nasopharynx which received a very heavy dose of supervoltage irradiation. Although this patient is alive and without obvious recurrence at 9 years after therapy, it is too early to be certain that there is no residual disease. The remainder of the cases occurring elsewhere than in the palate have died with extensive recurrence.

RESULTS OF TREATMENT BY SITE

TUMORS OF PALATE

Of 40 palatal tumors there were more than twice (25) as many mixed parotid tumors as cylindromas (11) (Table v).

Of 17 patients with mixed parotid tumors treated more than 5 years ago, 10 have not had recurrences and 4 are lost. Only 3 cases have known recurrence, but since only 7, 16 and 20 years have elapsed after treatment, it is possible that the disease may recur in some of the others. Two patients have died of other causes without disease at 5 and 8 years.

Even in the case of cylindroma the prognosis is more favorable when it occurs in the palate rather than elsewhere and only 3 of 9 such cases developed recurrences—all died of carcinoma at 3, 5 and 13 years, respectively. One patient of this group was first treated in 1944 by surgery and then 7 different times by irradiation for recurrences before dying of the disease 13 years later. In spite of intensive therapy, the neoplasm gradually spread, both locally and along the nerves to the base of the skull and pulmonary metastases also appeared as a terminal feature.

TUMORS OF THE PERITONSILLAR REGION AND LATERAL PHARYNGEAL WALL

In these regions the mixed parotid tumors predominate and the prognosis is therefore fairly good (Table VI). One patient with cylindroma in the peritonsillar region died of hemorrhage shortly after surgery. The 5 cases of mixed parotid tumors seen before 1957 all survived 5 years, although 2 ultimately died of the disease. One patient with a peritonsillar tumor, already mentioned, was first treated by surgery in 1924 and died 20 years later with metastases in the bones. The second patient had a pharyngeal wall tumor and died with a recurrence at the base of the skull after 7 years.

TUMORS OF THE MAXILLARY ANTRUM AND ETHMOIDS

In these areas cylindroma predominates and the prognosis is extremely bad (Table VII). Seven cases seen before 1958 have all had recurrences and of the 4 which survived 5 years, 3 died at 5, 7 and 10 years and 1 is alive with carcinoma 10 years after the first treatment. In this group of cases the cause of death is upward extension with involvement of the ethmoid regions, orbits and the base of the skull, presumably by infiltration along the fifth nerves. This has impressed upon us the importance of first treating with supervoltage roentgen or gamma rays and including the base of the skull in the radiation field. In these cases irradiation is followed by palatal antrostomy and also, when indicated, by ethmoidectomy or exenteration of the orbit. Since the introduction of supervoltage therapy, we have been encouraged to find a diminished incidence of residual growth at the time of operation.

TUMORS OF THE NASOPHARYNX AND NASAL CAVITY

In these inaccessible regions the results of treatment are disappointing even with less infiltrating tumors (Table VIII). Of 4 cases of cylindroma all have had recurrences and 3 of these have died at intervals of 4, 6 and 10 years from the time of the original treatment. The fourth patient with a cylindroma of the nasopharynx was treated by Professor Sir Brian Windeyer with the linear accelerator, a high dose being given to the base of skull and the nasopharynx, when there was already evidence of involvement of several cranial nerves. Now, 9 years after

TABLE VI

RESULTS OF TREATMENT OF TUMORS OF PERITONSILLAR REGION AND LATERAL PHARNYGEAL WALL 1928–1957

	1928–1962	1928–1957					
	Total Seen	Total Seen	No Recurrence	Recurrence	Lost	Five Year Survival	Later Developments
Mixed parotid type	6	5	3	2		5	Died of cancer—2 cases
Cylindroma	1*	1*					
Total	7	6	3	2		5	Died of cancer—2 cases

* Died after operation.

Table VII

RESULTS OF TREATMENT OF TUMORS OF MAXILLARY ANTRUM AND ETHMOIDS 1928–1957

	1928–1962	1928–1957					
	Total Seen	Total Seen	No Recurrence	Recurrence	Lost	Five Year Survival	Later Developments
Mixed parotid type	3	1		1 Died in 9 months			
Cylindroma	10	7		7 Died of cancer—3 cases (1, 1, 1 yr.)		4	Died of cancer—3 cases Alive with cancer—1 case
Mucoepidermoid tumor	1						
Carcinoma	2	2		2 Died of cancer—2 cases (1, 3 yr.)			
Total	16	10		10		4	Died of cancer—3 cases Alive with cancer—1 case

the first treatment, she is said to be well though with local necrosis.

Even the mixed parotid tumor cases do poorly in this site, where adequate excision is impossible, and their radioresistance makes them disappointing to treat by radiation therapy. Of 5 cases, 4 have had recurrence. One of these was lost 4 years after

Table VIII

RESULTS OF TREATMENT OF TUMORS OF NASOPHARYNX AND NASAL CAVITY 1928–1957

	1928–1962	1928–1957					
	Total Seen	Total Seen	No Recurrence	Recurrence	Lost	Five year Survival	Later Developments
Mixed parotid tumor	6	5	1	4	1	4	Alive with cancer—3 cases
Cylindroma	4	4		4 Died of cancer—1 case (4 yr.)		3	Died of cancer—2 cases
Total	10	9	1	8	1	7	Died of cancer—2 cases Alive with cancer—3 cases

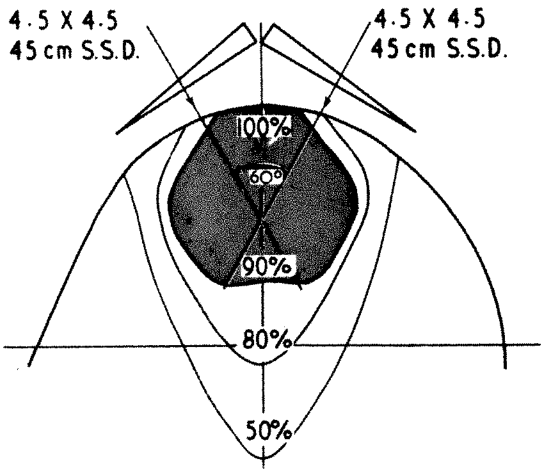


Fig. 1. Theratron wedge fields. Common combinations of wedges used at Middlesex Hospital: 100 rads incident dose on both fields gives a combined dose of 137 rads to the 90 per cent and 122 rads to the 80 per cent level.

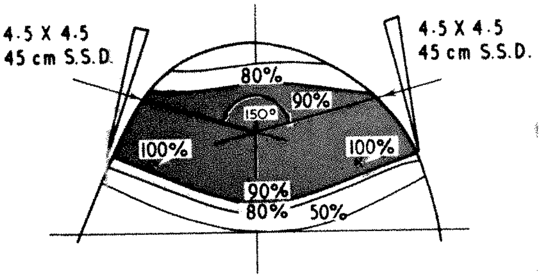


Fig. 3. Theratron wedge fields. Equal doses to each field: 100 rads incident dose on both fields gives a combined dose of 130 rads to the 90 per cent and 114 rads to the 80 per cent level. Note symmetric arrangement with rapid fall off outside high dose volume.

treatment, 1 is apparently well at 15 years and 3 are alive with evidence of disease at 9, 14 and 15 years, respectively, after the original treatment.

DISCUSSION

We feel that patients with mucous gland tumors should receive intensive initial treatment by surgery or radiation therapy or by a combination of both and that the treatment policy must be decided and reviewed at a combined clinic attended by surgeons and radiotherapists.

In tumors of the mixed parotid type, wide excision with a good margin of normal tissue is the treatment of choice but where, owing to the extent or site of the tumor, such excision is not possible a preoperative course of radiation therapy is given. In the cylindroma cases preoperative irradiation is the rule and a larger volume is treated which always includes the line of the nerves and the base of the skull. Wherever possible a wide excision is performed 6 or 8 weeks after the end of radiation therapy.

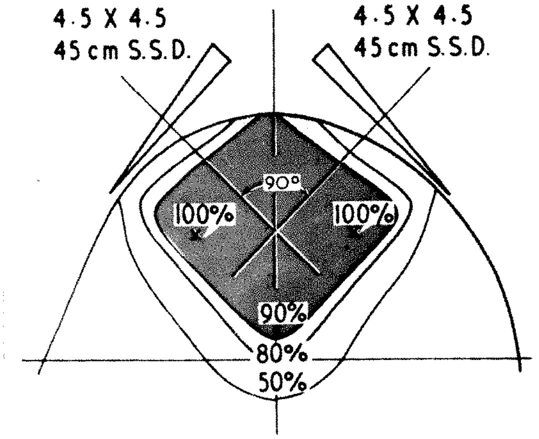


Fig. 2. Theratron wedge fields. Equal doses to each field: 100 rads incident dose on both fields gives a combined dose of 133 rads to the 90 per cent and 120 rads to the 80 per cent level.

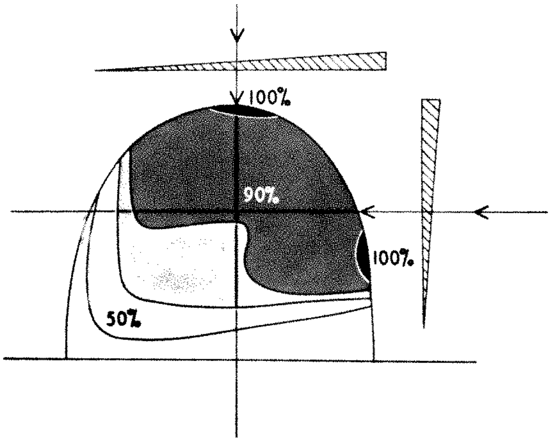


Fig. 4. Carcinoma of tongue. Junior Theratron; source skin distance 45 cm.; wedges at a right angle: equal incident doses but unequal field size. Note drop from 90 per cent to 80 per cent in remote corner; additional small unwedged fields are often used to raise the dose at this point.

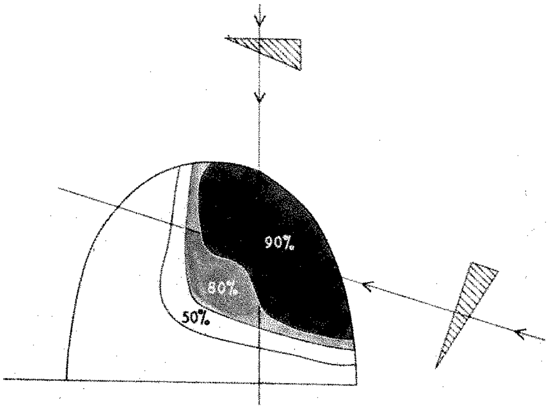


Fig. 5. Carcinoma of floor of mouth. Junior Theratron; source skin distance 45 cm. A wedge arrangement often used for disease in the floor of the mouth or in the neck. Note again the drop from 90 per cent to 80 per cent medially and posteriorly which may, unless corrected, produce a dangerous low-dosage area.

In all cases supervoltage techniques are used. A dosage of 5,000 to 6,000 rads is given over about 6 weeks to patients with mixed parotid tumors, while those with cylindromas receive 6,000 to 7,000 rads over a period of 6 to 8 weeks.

TECHNIQUES USED AT THE MIDDLESEX HOSPITAL

The patients are treated with gamma rays from cobalt 60 sources. Treatment is given either on the Mobaltron with a source skin distance of 60 to 70 cm. or on the Theratron with a source skin distance of 40 to 50 cm. Most cases of tumors of the head and neck are treated on the Theratron and special techniques have been devised to cut down the penumbra around any part of the treatment area where it is desired to protect sensitive normal tissues.

Gamma rays are used primarily because of the presence of bone and cartilage in the irradiated volume; however, the skin sparing effect is also regarded as valuable in these patients, who are often relatively young and can survive the treatment for at least a number of years. Wedge techniques are usually employed since they make it possible to give relatively homogeneous

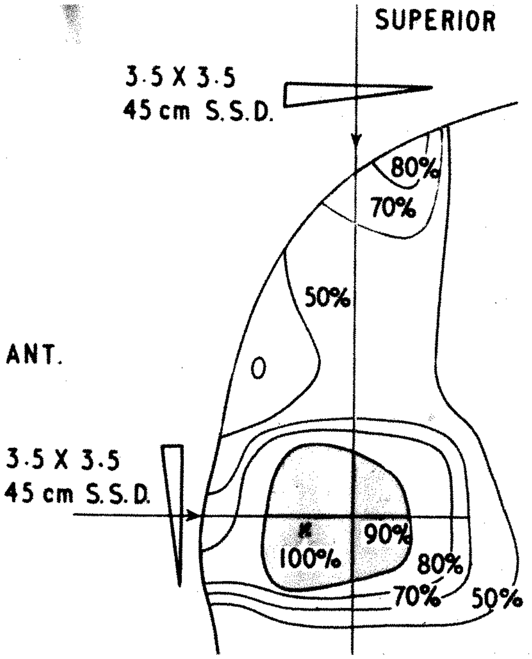


Fig. 6. Theratron. Sagittal outline through center of the orbit. A technique used for treating the orbit by superior and anterior wedge fields which allows adequate protection of the contralateral orbit. Note the effect of using two wedged beams with the same source skin but different source tumor distances: 100 rads incident dose on both fields gives a combined dose of 99 rads at the 80 per cent level.

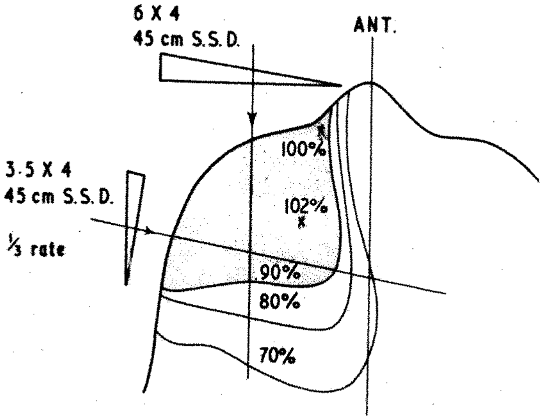


Fig. 7. Theratron. Transverse outline through center of orbit. The shape of the high dose volume may be altered by giving unequal doses to two wedged fields: 100 rads incident dose on the anterior field plus $33\frac{1}{3}$ rads incident dose on the lateral fields gives a combined dose of 90 rads to the 90 per cent level.

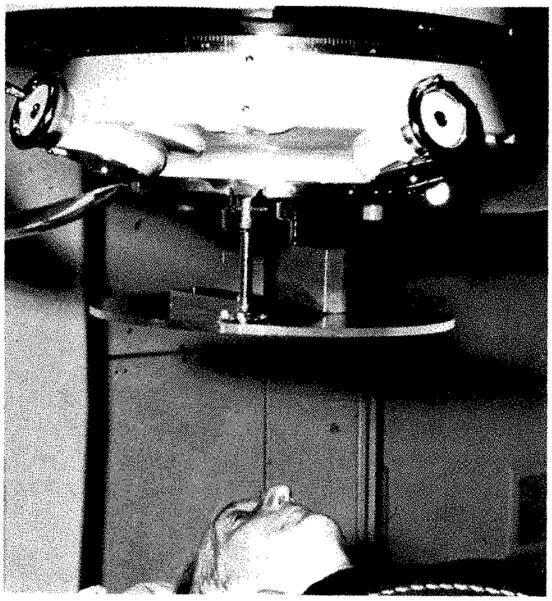


Fig. 8. Technique first used on the Mobaltron. The steel wedge is screwed to a plastic tray suspended from the head of the Mobaltron. Lead blocks placed on the tray protect the contralateral orbit. This technique can be used only with a vertical beam.

irradiation to the desired volume, while the quick fall-off around this spares adjacent normal tissues. Of special importance in these cases is the protection of the eyes, brain and spinal cord, but we also try to avoid unnecessary irradiation of the oral and nasal cavities in unilateral disease. Figures 1 to 7 show plans commonly used in this type of treatment at the Middlesex Hospital and it can be seen how by altering the size of the wedges, the angle between them and the dose delivered to each, the shape of the high dosage volume can be altered to provide the required distribution. It is also obvious that, while the abrupt fall in the dose at the edge of the treated volume is an advantage in that the normal tissues are spared, there is a danger that unless absolute precision of treatment can be achieved some part of the tumor may receive inadequate treatment.

Since collimation is not adequate for the protection of adjacent, very sensitive, normal structures where these lie close to the tumor—for example, the contralateral eye in a case of neoplasm involving the ethmoid cells—additional protection is provided by the suspension of a 7 cm. long and 1 cm. wide lead plate from the applicator base that holds the wedge and is inserted into

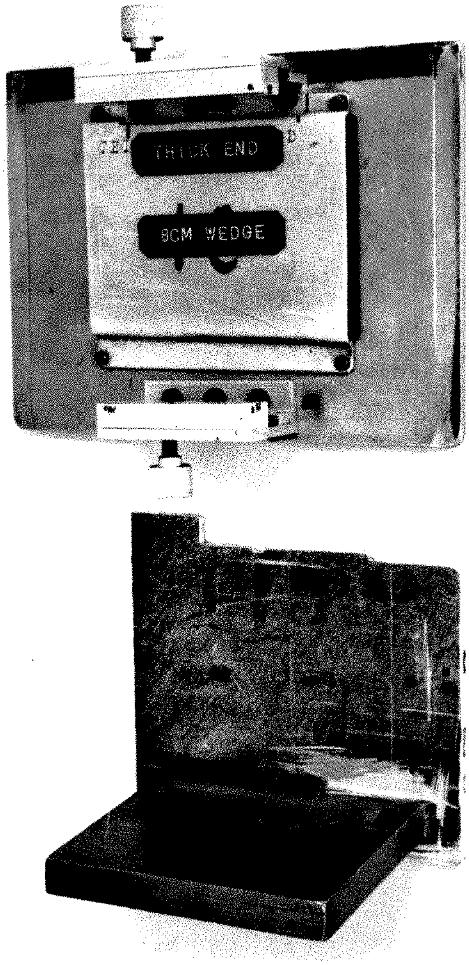


Fig. 9. Wedges are now fixed to applicator bases to which are also attached vertical lead shields which protect radiosensitive adjacent structures. A compensator can also be constructed on the same base.

the applicator housing (Fig. 8–10). This affords adequate protection since the rays pass obliquely down it and it is our practice to provide each patient with a special applicator base which is attached to the wedge and the lead plate, both specially adapted for the field size to be used.

The Meyerstein Institute of Radiotherapy
The Middlesex Hospital
London, England

I should like to thank Dr. A. C. Thackray, Dr. J. N. Pattinson, and Mr. C. P. Wilson for permission to quote their papers. In every instance the histologic report has been rechecked by Dr. A. C. Thackray. I am grateful to them and to Professor Sir Brian Windeyer, Dr. A. M. Jelliffe, Mr. Douglas Ranger and other colleagues for their assistance with this paper and for permission to report cases under their care.

I am also indebted to Mr. T. Bryant, Miss I. Hoppett and Miss A. Deubert in the Physics Department for their advice and collaboration in plans and treatment methods and to Mr. S. Beare, Medical Adviser to the Records and Art Department, for advice on many points. I would also like to thank Mr. T. E. Cowan, the Records Officer, for help in compiling this survey and Mr. M. S. Turney, the Medical Photographer, and Mr. H. S. Drury, the Medical Artist, for all their careful work on the illustrations.

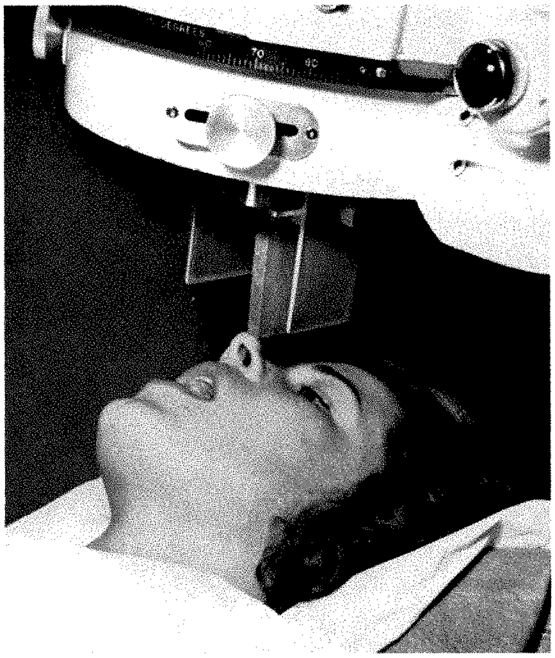


FIG. 10. Carcinoma of the right antrum treated with the Theratron. A vertical lead plate protects the left eye. The mouth is kept open with a gag to remove the tongue and lower jaw from the neighbourhood of the beam.

REFERENCES

1. RANGER, D., THACKRAY, A. C., and LUCAS, R. B. Mucous gland tumours. *Brit. J. Cancer*, 1956, *10*, 1–16.
2. THACKRAY, A. C., WILSON, C. P., PATTINSON, J. N., and SNELLING, M. D. Symposium on mucous gland tumours. *Clinical Radiology*, 1961, *12*, 241–268.

AN UNUSUAL CASE OF RADIUM TOXICITY[*]

By H. F. LUCAS, JR.,[†] R. E. ROWLAND,[‡] C. E. MILLER,[†] R. B. HOLTZMAN,[†]
R. J. HASTERLIK,[§] *and* A. J. FINKEL[‖]
ARGONNE, ILLINOIS

AN UNUSUAL case of radium toxicity was discovered in the course of a study of radium levels in bone in known cases of osteogenic sarcoma in man. Bone from individuals with such sarcomas was obtained from the collection at the Mayo Clinic, Rochester, Minnesota, through the courtesy and cooperation of Dr. D. C. Dahlin. Normal total body radium levels, as a result of ingestion of food and water, are in the range of 10^{-5} to 10^{-8} μc Ra^{226}. The first estimate for this case yielded a total skeletal content of 0.14 μc, a value well above the normal environmental range, but very nearly equal to the MPC of 0.1 μc. Consequently, this case presented an extremely interesting problem and the results of further investigations are presented here as a separate study.

At the time of the initial radiochemical analysis of the bone sample that had been acquired after a mid-femoral amputation of the leg, the patient was still alive, but in very poor health. We were able, however, to make total body gamma-ray and radon breath measurements, and to collect a series of fecal samples. After her death which occurred a short time later, a piece of bone from the opposite femur was made available for study.

REPORT OF A CASE

The patient, a 54 year old married white woman, was studied by our group in 1961 during the last 5 months of her life. She was born in South Dakota and at the age of 4 moved to western Oregon where she spent the remainder of her life. She had never been pregnant. Previous medical history included appendectomy at age 18 years, unilateral ovariectomy at age 23, complete hysterectomy at age 35, and excision of a benign tumor of the posterior neck at age 48.

Painful discomfort in the left knee developed during the summer of 1958 (age 51). Roentgenograms disclosed a destructive lesion on the posterior aspect of the lower femur immediately superior to the medial epicondyle. Surgical excision of the lesion and replacement of the defect by bone chips were performed in November, 1958. Because of recurrent pain, the affected area was biopsied and the lesion was again thought to be nonmalignant. Pain increased, the lesion was explored a third time in June, 1959, and the graft was removed by curettement. Within a month, roentgenograms showed massive proliferation of aberrant bone at the site of the original lesion; it was now thought to be an osteosarcoma. Amputation through the upper end of the femur was performed in October, 1959, at the Mayo Clinic. The pathologic report, furnished by Dr. Dahlin, gave a diagnosis of "Grade 3 osteoblastic osteogenic sarcoma." By October, 1960, pulmonary metastases were present, and the patient died on October 28, 1961.

We interviewed the patient and measured her for whole-body radium content on June 7, 1961 in the home of her physician. She had no occupational history of exposure to radium, having worked as a waitress, store clerk, and office employee. She could not recall ever taking radium by mouth or receiving it by injection.

Roentgenograms were made available to us for the period 1959 to 1961. Apart from the tumor, roentgenograms of the left knee and leg taken in June, 1959 revealed definite coarsening of trabeculation of the tibia and fibula, multiple areas of bone resorption measuring up to 2 cm. in length in the shaft of the tibia, and a 1 cm. area of bone resorption in the distal femur 5 cm. proximal to the tumor. Areas of bone resorption and marked thickening of the calvarium were seen on the lateral roentgenograms of the skull taken in June, 1961. Multiple areas of bone resorption measuring up to 1 cm. in diameter were also noted at this time in the medial epicondyle of the left humerus. In addition, there was marked thickening of the cortices of the radius and ulna bilaterally. These roentgenographic findings were typical of those seen following long term deposition of radium in the skeleton at levels in the whole body above 0.4 μc.[4,9] The observation that the old distal epiphyseal line of the left radius was accentuated and sclerotic led to the impression that the patient might have received radium at about 18 years of age.

---

[*] This case is numbered 03-216 in the Argonne series of radium cases. This work was performed under the auspices of the United States Atomic Energy Commission.

[†] Radiological Physics Division, Argonne National Laboratory, Argonne, Illinois.

[‡] Present address: University of Rochester, School of Medicine and Dentistry, Rochester, New York.

[§] Argonne Cancer Research Hospital, Chicago, Illinois.

[‖] Health Division, Argonne National Laboratory, Argonne, Illinois.

Shortly before the patient died she recalled that she had consulted a dermatologist in a large city in the Pacific Northwest in 1922 or 1923 (age 15 or 16 years) for the treatment of psoriasis. She received a series of weekly injections and had a prescription for a pink liquid that was taken by mouth. We made an attempt to trace the records of the dermatologist, who had died in 1948, but we were not successful. Nor were we able to determine if radium had been prescribed for the patient by a search of the records of the pharmacy where the prescription had been filled. Consequently, we have no direct evidence bearing on the source of the radium that was measured *in vivo* and in various specimens of bone that were made available to us.

WHOLE BODY GAMMA-RAY MEASUREMENTS

The patient was measured for radium content in the home of her physician by means of portable equipment which consisted of a 3 inch diameter by 5 inch long NaI(Tl) crystal, a 256-channel transistorized analyzer,* and a Hewlett-Packard printer.†

Three different whole body measuring techniques were used. Physical descriptions of these techniques and their probable accuracies have been published elsewhere.[15] The first arrangement was an adaptation of the tilting chair technique used in the whole body counter at Argonne National Laboratory. The patient was seated in an ordinary lawn chair with plastic webbing, and the 3×5 inch crystal was located 42 cm. above the seat of the chair and 42 cm. in front of the back of the chair. The axis of the crystal was tilted 45 degrees from the vertical and pointed at the patient's pelvis (Fig. 1, crystal position 1). Since the counting rate obtained with this technique in an unshielded room was very little above background, two additional measuring techniques were used in an effort to improve the accuracy of the measurement.

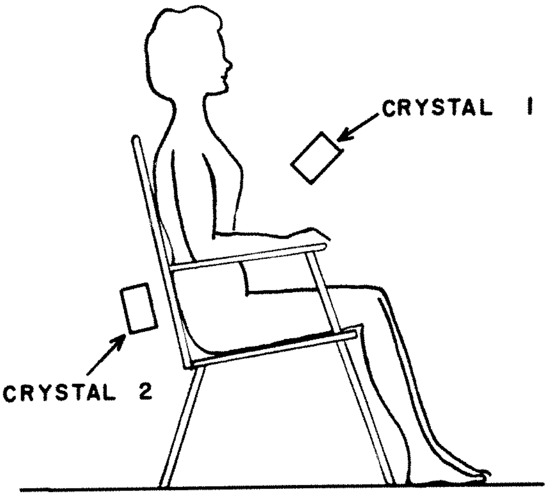


Fig. 1. Diagram showing arrangement of crystals and patient for gamma-ray spectroscopy.

In the second technique, the patient was seated in the same lawn chair but the crystal was placed behind the chair at the level of the lumbar spine. The crystal was positioned with its axis parallel to the patient's vertebral column 10 cm. from the back of the chair and with the top of the crystal 60 cm. from the floor (Fig. 1, crystal position 2).

The third technique is a modification of a four crystal array in that four separate measurements were made with the same crystal. The crystal with its axis vertical and with its face 21 cm. above the surface of the bed was placed at each of four locations above the mid-line of the supine patient. These four positions were centered over the nose, the sternum, the pelvis, and the patella.

It was necessary to measure normal subjects in the same position as the patient,

---

* Technical Measurements Corporation, Model CN-110.
† Technical Measurements Corporation, Model HP-561B.

TABLE I

RA B AND RA C CONTENT MEASURED BY γ-RAY SPECTROMETRY

Technique 1		0.169 μc
Technique 2		0.115 μc
Technique 3		
Over nose	0.105 μc	
Over sternum	0.161 μc	
Over pelvis	0.152 μc	
Over knee	0.127 μc	
Mean		0.136 μc
Mean of Three Techniques		0.140 μc

since her body shielded the crystal from the naturally present gamma-ray background. While these persons were uncontaminated with radium, they contained Cs^{137} and K^{40}, and this procedure corrected for the gamma-ray contributions from these two elements. Inasmuch as these elements may contribute as many gamma-ray counts as 0.01 μc Ra B and Ra C, this correction was considered to be of importance.

The calibration factors used to calculate the amount of radium by the chair techniques were determined by counting 2 other patients whose body content of radium had been accurately measured in the whole body counters at Argonne National Laboratory and at Massachusetts Institute of Technology. The portable equipment was set up in each of these patients' homes where the patient and an uncontaminated person were measured. The calibration factor in counts per minute per μc Ra B and Ra C was found by dividing the counting rate of the contaminated patient (after subtracting that of the uncontaminated subject) by the amount of radium known to be present from previous measurements. For the third technique, similar calibration factors were derived for each of the four crystal positions by measuring two supine subjects within the low background, shielded room at Argonne National Laboratory. One of these patients had also been measured in the two previously mentioned whole body counters. The quantity of Ra B and Ra C expressed in μc calculated by each crystal position technique is given in Table I.

The values given in Table I for the three techniques agree reasonably well. The first and third yielded values within 11 per cent of their average of 0.152 μc of Ra B and Ra C. The second technique yielded a value of 0.115 μc or 25 per cent less than the average of the other two methods.

On the basis of these whole body measurements, we estimated that this patient contained about 0.15 μc of Ra B and Ra C in her body. If on the basis of previous studies we assume that 69 per cent of the radon formed in her body was lost by exhalation, then the body content of Ra^{226} was 0.49 μc. Correction for the absent leg as a result of mid-thigh amputation would bring this value to 0.60 μc Ra^{226} for the entire body. This calculation is based on an estimated loss of 18 per cent of the mass of the skeleton as a result of the surgery.[22]

Previous experience has shown that the first and third techniques have inherent uncertainties of about 10 per cent due to variability in radium deposition in the human skeleton,[15] while the second method has an error at times as large as two-fold, and is therefore less reliable.

RADIOCHEMICAL ANALYSIS

The first sample of bone from this subject was a complete cross-section of the mid-femur. It was from an apparently normal area of bone adjacent to the tumor. This sample of bone (410B-1) had been stored in formalin for about 1 year and was still wet on receipt. Negligible leaching of radium by the formalin had occurred. The specimen was dried at 100° C., split into three longitudinal sections, and the marrow was washed from the bone with ether and a small brush. One of these pieces (approximately a one-third cross-section) was ashed at 600° C. in a platinum crucible, dissolved in 14.7 ml. conc. HNO_3, and diluted with water to 40 ml. The thorium was ex-

TABLE II

Ra^{226}, Th^{228}, AND Ra D CONTENT OF BONE

Sample No.	Date Taken	Sample Size (g. ash)	Ra D pc/g. ±E[1]	Th^{228} pc/g. ±E[1]	Ra^{226} pc/g. ±E[1]	Ra^{226} Extrapolated Whole Body[2] (µg.)
410B-1	10/5/59	8.32		0.002±0.001	53.1±0.5	0.14
	10/5/59	0.204	42.1±1.1	—	149±2	0.39
	10/5/59	0.254	35.0±0.7	—	122±2	0.32
	10/5/59	0.197	26.4±0.5	—	88±2	0.23
410B-2	10/28/61	1.72	—	—	267±5	0.69
Mean						0.4

[1] 0.9 statistical counting error.

[2] Assuming 2,600 g. ash per skeleton.

tracted into dibutyl phosphate by the technique of Stehney *et al.*[23,24] and the Ra^{226} was determined by the emanation technique and counting system of Lucas.[10,11] Ra D was determined on a section of wet-ashed bone by plating the Ra D daughter, Po^{210}, onto silver and counting the deposited alpha activity.[6,7] The second sample (410B-2) obtained from the contralateral femur after death was analyzed in a manner identical to the first.

The data from these analyses are summarized in Table II. The Th^{228} content of 0.002 pc/g. ash was nearly identical to the 0.003 pc/g. ash found in bone from persons whose only source of Ra^{226} and Ra^{228} was food.[12] This very low content of Th^{228} is further evidence that the very large concentration of Ra^{226} in the patient could not have been obtained from natural food and water sources.

The concentration of Ra^{226} in the second sample obtained after death was nearly 5 times that of the 8.3 g. piece of the first sample. This difference between homologous bones is attributable to the nonuniform distribution of the radium in the bone as shown by autoradiography (*vide infra*).

The Ra D was found to vary by a factor of about 2 for the three small portions of bone. The ratio of Ra D to Ra^{226} was, however, remarkably constant at 0.28 with a standard deviation of ±0.01. This value, when considered along with previously published measurements of Ra D in persons with a high radium content,[8] is consistent with the estimate that the radium had been acquired 35 to 40 years previous to measurement and that the average radon retention was about 40 per cent. The latter figure is in fair agreement with other earlier estimates of whole body radon retention of 31 per cent found after 30 to 35 years.[14]

Fecal samples were obtained for a 5 day period in August, 1961 approximately 2 months before death. The Ra^{226} content of these samples is summarized in Table III. Each sample represents a single bowel movement except No. 100F1 which represents two. The average daily Ra^{226} excretion (35.4 pc/day) divided by the observed body burden of about 0.5 µc gives a coefficient of daily elimination of 7×10^{-5}. This is almost identical to the average of 10 cases for which Norris *et al.*[16] found a value of 8×10^{-5}. The dry weight and calcium content of these fecal samples, although somewhat low, are within normal limits.

The Ra D present in these fecal samples averaged about 1 pc/day and is within the normal limits of 1 to 2 pc/day obtained from food and water.[8] The contribution of a whole body Ra D content of 0.2 µc would

TABLE III

Ra^{226} IN FECAL SAMPLES, CASE NO. 03-216

Sample No.	Date of Collection	Weight Dry	Ash (g.)	Calcium (g.)	Ra^{226} pc ± E*	Ra D pc ± E*
100F1	8/15/61	23.1	1.60	0.104	52.1 ± 1.1	0.96 ± 0.04
100F2	8/16/61	15.7	1.17	0.113	36.6 ± 0.9	1.11 ± 0.04
100F3	8/17/61	11.4	1.11	0.124	33.3 ± 0.7	1.17 ± 0.05
100F4	8/18/61	10.0	0.77	0.074	26.2 ± 0.5	0.76 ± 0.04
100F5	8/19/61	19.7	1.02	—	28.8 ± 0.4	—
100F6	Blank	8.7	0.00	—	0.01 ± 0.01	—
	Average	14.4	1.13	0.104	35.4	1.00 ± 0.18

* 0.9 statistical counting error.

not be detectable in the feces unless the Ra D content of the food intake were very accurately known.

In order to measure the amount of radon being exhaled from the patient's body, a single 10 liter breath sample was collected from both the patient and from a control subject. A net radon concentration of 1.74 pc/l. was found after correcting for a room air blank of 0.09 pc/l. This radon content normally would indicate a total body radium content of about 0.17 μc of Ra^{226}.[1] This breath sample therefore indicated a body content one-third of that found by gamma-ray measurements. Breath samples obtained from other patients have demonstrated that the radon concentration in any *single sample of this type* may vary from the average by a factor of 2.

AUTORADIOGRAPHIC AND MICRORADIOGRAPHIC STUDIES

The microradiographs of material cut from a one-third segment of a cross-section of the femur verified that this was in fact bone from a patient suffering from radium poisoning.[21] Many plugged haversian canals, hypercalcified areas, and typical "moth-eaten" areas that characterize radium-containing bone microradiographically were present. However, these microradiographic signs were not uniformly distributed throughout the bone sections, some of the areas showing very few such signs, others showing many such signs.

The radium content of the diffusely labelled areas was determined from autoradiographic alpha track plates exposed for 28 days. From such measurements a good estimate of total skeletal radium content can be made, since the diffuse level in other radium cases averages about 50 per cent of the hypothetically uniform label, *i.e.*, the skeletal radium content divided by the total skeletal mass.[20] These first measurements of diffuse and hot spot radium concentration are listed in Table IV.

From these measurements it was calculated that this diffuse distribution was characteristic of a total body radium content of about 2 μc. In addition, it has been possible to estimate from the observed data the route of acquisition of the radium,

TABLE IV

DIFFUSE AND HOT SPOT MEASUREMENTS OF BONE SAMPLE 410B-1

Section	Diffuse Level (pc Ra^{226}/mg. bone)	Hot Spot Level (pc Ra^{226}/mg. bone)	Predicted Body Content (μc)*
1-3	0.11	—	1.3
2-3	0.20	—	2.4
2-9	0.20	—	2.4
2-6	0.21	36.4	2.4
Hot Spot to Diffuse Ratio = 180			

* Based on a 60 kg. body mass, 6 kg. bone, diffuse 50 per cent of uniform label.

the total quantity acquired, and the length of time over which it was acquired. It would appear that this patient received Ra^{226}, probably via the intravenous route, for a period of 3 months or less, and that she was given between 300 and 400 μc Ra^{226}.

These conclusions were based on the following observations: The "hot spot" to diffuse ratio of 180:1 is suggestive of a relatively short acquisition time. Thus the medical route is more likely than occupational exposure since no former radium dial painter has yet been studied who had a ratio this high. Two Elgin State Hospital patients, with acquisition times of 7 and 18 weeks, had ratios of 263:1 and 218:1, respectively.[19] Subsequent examination of high resolution strip films has given a more accurate estimate of the short acquisition period, for they show the alpha tracks to be concentrated in bands 50 to 80 microns wide. At a linear growth rate of 1 micron/day,[5] the exposure would have been limited to less than 3 months.

The maximum "hot spot" concentrations in the Elgin State Hospital patients studied average 14 pc/mg. bone in persons who had received 10 μc Ra^{226} per week intravenously.[19] The level of 36 pc/mg. observed here is about 3 times as great, so that about 30 μc Ra^{226} per week intravenously would be required to have produced "hot spots" at this level. Thirty microcuries per week for 12 weeks yields a total input of 360 μc. Had this isotope been given orally, a much greater quantity would have been required to produce the observed concentrations as a consequence of the discrimination factors controlling absorption of radium from the gastrointestinal tract.

The power law has been proposed as a valid description of radium retention.[17] On the assumption that the radium was acquired about 30 years ago, a total input of 360 μc would have left 1.6 μc terminally, according to a power function of $R = 0.54\ t^{-0.52}$. This value is in good agreement with the level of 2 μc suggested by autoradiography.

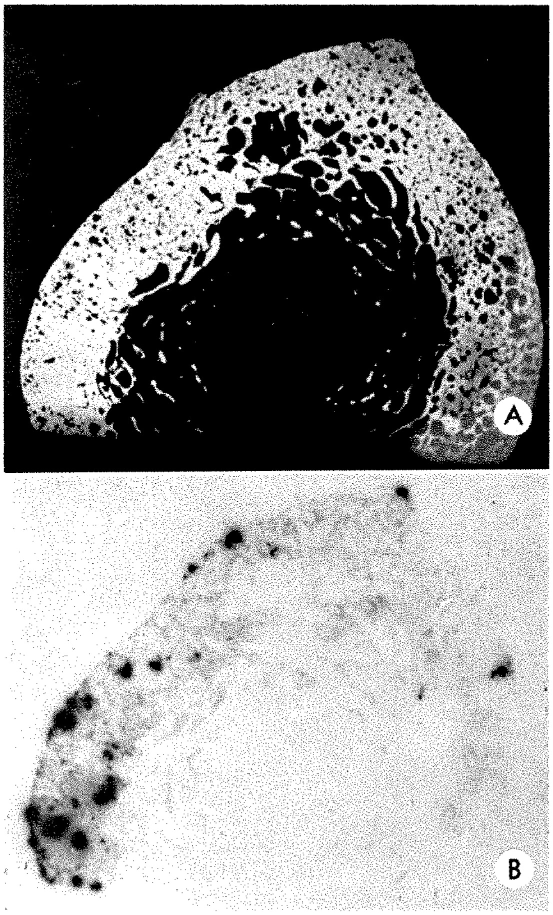


Fig. 2. (*A*) A microradiograph and (*B*) an autoradiograph of 100 μ thick cross-section from the amputated femur of case 03-216. The autoradiograph was exposed for 1 year on Type A autoradiographic plate.

A gross autoradiograph (Eastman Kodak Autoradiographic Type A) of a segment of the amputated femur was developed after an exposure of 1 year and is shown, with a microradiograph of the section, in Figure 2 *A* and *B*. It is apparent that the diffuse distribution of radium in this bone is not uniform.

Subsequently, a complete cross-section from the amputated femur was obtained for autoradiographic study. When these autoradiographs (Fig. 3, *A* and *B*) were examined, it was found that about one-half of the bone section contained a much lower diffuse radium level than the other. Alpha

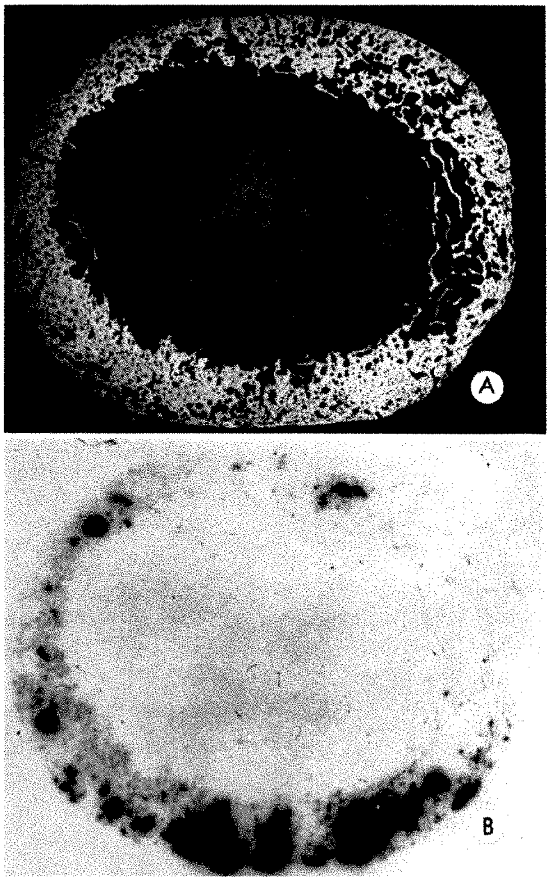


FIG. 3. (*A*) A microradiograph and (*B*) an autoradiograph of a $150\ \mu$ thick section from the amputated femur of case 03-216. This 1 year autoradiograph shows considerable evidence of remodelling in several locations.

track counts over these two regions indicated that the lower level contained 4 per cent of the concentration found in the higher diffuse level.

It was concluded that considerable bone turnover had occurred during the time interval between the acquisition of radium and the amputation. The new replacement bone contained radium at a very low level, determined by the level of the radium in the blood at the time the new bone was formed. The amount of bone turnover was remarkably high as indicated by the quantity of bone that was relatively radium free. Of approximately the 30 radium cases studied autoradiographically in this laboratory,[18] only one, No. 01-008, approached this level of bone turnover. The other cases appeared to have bone turnover that was of an order of magnitude lower for equivalent exposure intervals.

It should be recalled that the chemical determination of the radium content of a complete cross-section of this bone (Sample 410B-2) gave a result 5 times as large as the first determination done on a one-third segment of a femoral cross-section (Table II). From Figure 3, *A* and *B* it is easy to visualize how a one-third segment could have missed the higher concentrations present in the complete cross-section and emphasizes the necessity of working with complete cross-sections of bone from as many skeletal sites as possible.

DISCUSSION

This case was pursued with tenacity because of the important implications of the available information. At the beginning of this investigation, the body content was estimated to be 0.14 μc by extrapolation from a radiochemical analysis of a small piece of bone. This value is much lower than that found in any other radium patient with a malignant bone tumor. Unfortunately, the patient and her physicians were unaware that she carried a large amount of radium and thus were not able to provide any information concerning its acquisition. There are still many hundreds of people in the United States who carry a significant amount of radium in their body. Consequently, the techniques described herein to establish the date, route, and amount of radium exposure will have application in the future.

The radium in the patient, exclusive of the amputated leg, was determined by whole body gamma-ray spectroscopy to be 0.5 μc. Estimates have also been obtained by a variety of other methods. By extrapolating to the whole skeleton, from radiochemical measurements of the radium contained in small pieces of bone, estimates ranging from 0.14 to 0.69 μc were obtained. While comparable measurements have not been made for a single whole bone, a similar range of values has been found by Norris *et al.*[16] on small samples from many different bones from the same individual. Only one radon breath sample was obtained from our patient and it is not possible to evaluate the accuracy of this determination. Estimates from autoradiographs were very much higher and ranged from 1.3 to 2.4 μc. As will be discussed later, these high estimates are related to abnormally large fractions of the skeleton which have been removed and replaced with bone having very low levels of radium.

By elimination of various possible sources of exposure such as natural acquisition and industrial exposure, it was shown that the route must have been by intravenous injection. Study of the autoradiographs suggests that the radium was given in a period of about 3 months or less and that a total dose of about 360 μc Ra^{226} was administered. The diffuse radium levels that were observed in areas of bone not remodelled since the time of acquisition are characteristic of a terminal body content of 2 μc radium. This estimate is in agreement with what would be predicted by comparison with radium retentions observed in the Elgin series.[14] These inferences were made before we received the information that the patient did indeed have a series of weekly injections of an unknown medication in 1922 to 1923. Although we surmise that these injections may have been radium, this supposition is not supported by direct evidence.

The date of intake was estimated from several observations. The marked thickening of the cortices of the radius and ulna and the accentuated epiphyseal line of the left radius are both characteristic of radiation damage during the period of rapid skeletal growth. The ratio of fecal radium to measured body radium content (0.5 μc) is essentially the same as that found in other patients who received radium 20 to 40 years earlier.[13,16] On the assumption that Ra D was entirely a daughter product of the Ra^{226} deposited in the bone, the Ra D/Ra^{226} ratio in the bone was also consistent with a 40 year residence time of radium in this patient.

If the estimate of terminal body content from the autoradiographs is high by a factor of about 3 (2/0.6), then the initial injected dose may have been 120 μc rather than 360 μc. This amount could readily have been acquired by weekly injections of 10 μc (the usual treatment dose) over a 3 month period and is a value that is reasonable since 10 μc ampules were then commercially available and are known to have been administered for a variety of medical conditions.[9]

On the other hand, another explanation of the apparent discrepancy may be obtained from the study of the autoradiographs (Fig. 2*B* and 3*B*). The diffusely labelled areas of bone are not as uniform as are found in the usual radium case. The radium contained in large areas of bone that appear to have little or no radium has been determined by alpha-track counting, and is 4 per cent of the diffuse and 0.02 per cent of the "hot spot" concentrations. Thus, large areas of bone appear to have been resorbed and replaced by essentially radium-free bone many years after radium intake. The remaining, original bone has a radium content and distribution characteristic of a 2 μc total body radium. Presumably, sufficient bone throughout the skeleton had been resorbed and replaced to reduce the retained amount of radium to only 0.6 μc. This high degree of bone remodelling may be related to the early surgical induction of menopause at the age of 35 years.

Finally, the frequency of injection and the assumed early age at which the radium was administered may be significant factors. Thus, the damage in this case may have been more severe per unit of retained radium than in other cases studied. It appears that whereas the actual terminal body content was about 0.6 μc, the degree of radiographically observed damage was comparable to a content of 2 μc in other radium patients.

CONCLUSION

Although considerable attention is being given to terminal body content of radium, it may very well be that the initial amount of radium in the body is a more important factor in the carcinogenic process than terminal body content at the time the tumor is present.[2,3] The significance of this case in evaluating the carcinogenicity of radium in man lies in its contribution to the total body of knowledge of this subject, especially in its demonstration of methods for recreating the past history of the exposure. This case, accordingly, has to be considered along with the large series of cases that are currently under investigation by several groups in the United States and abroad. It would be unwise to generalize from the data of this particular case alone. It is presented as an example of the many types of analyses that can be brought to bear on this interesting and important problem.

H. F. Lucas, Jr.
Argonne National Laboratory
9700 South Cass Avenue
Argonne, Illinois

The authors are grateful to Drs. D. C. Dahlin, M. M. D. Williams, and A. L. Orvis of the Mayo Clinic for the original bone sample and for providing us with additional material and information. We are very grateful to Dr. George Drost for his kindness and cooperation in making this case available for study, and to Drs. B. Goldberg and A. L. Ovregaard for providing radiographs for examination. Thanks are due F. H. Ilcewicz, R. E. Jenkins, F. Markun and J. E. Farnham for the many analyses which they made and to L. D. Marinelli and J. E. Rose for their interest and encouragement.

REFERENCES

1. Evans, R. D. Protection of radium dial workers and radiologists from injury by radium. *J. Indust. Hyg. & Toxicol.*, 1943, *25*, 253–269.
2. Finkel, M. P., Bergstrand, P. J., and Biskis, B. O. Latent period, incidence, and growth of Sr^{90}-induced osteosarcomas in CFI and CBA mice. *Radiology*, 1961, *77*, 269–281.
3. Finkel, M. P., Biskis, B. O., and Bergstrand, P. J. Radioisotope toxicity: significance of chronic administration. In: Radioisotopes in the Biosphere. R. S. Caldecott, and L. A. Snyder, Editors. University of Minnesota Press, Minneapolis, 1960, pp. 461–473.
4. Finkel, A. J., Miller, C. E., and Hasterlik, R. J. Late effects of radium deposition in dial painters. *Radiation Res.*, 1959, *11*, 442–443.
5. Frost, H. H. Lamellar osteoid mineralized per day in man. *Henry Ford Hosp. Med. Bull.*, 1960, *8*, 267–272.
6. Holtzman, R. B. Measurement of the natural content of RaD(Pb^{210}) and RaF(Po^{210}) in human bone—estimates of whole-body burdens. *Health Physics*, 1963, *9*, 385–400.
7. Holtzman, R. B. Some determinations of the RaD and RaF concentrations in human bone. Argonne National Laboratory Radiological Physics Division Semiannual Report, January-June, 1960, ANL-6199, 94–118.
8. Holtzman, R. B. RaD(Pb^{210}) in human skeleton: estimates of exponent of retention function, skeletal content, and dose rate in high-radium people. *Radiology*, 1963, *80*, 122–123.
9. Looney, W. B., Hasterlik, R. J., Brues, A. M., and Skirmont, E. Clinical investigation of chronic effects of radium salts administered therapeutically (1915–1931). Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1955, *73*, 1006–1037.
10. Lucas, H. F., Jr. Improved low-level alpha scintillation counter for radon. *Rev. Scient. Instruments*, 1957, *28*, 680–683.
11. Lucas, H. F., Jr. Correlation of natural radioactivity of human body to that of its environment: uptake and retention of Ra^{226} from food and water. Argonne National Laboratory Radiological Physics Division Semiannual Report, January-June, 1961, ANL-6297, 55.
12. Lucas, H. F., Jr., Stehney, A. F., and Wallace, D. E. In preparation.
13. Lucas, H. F., Jr. Unpublished data.
14. Marinelli, L. D., Miller, C. E., and Lucas, H. F., Jr. Retention of radium in man from twenty to twenty-nine years after intravenous administration and some of its physiologic implications. *Radiology*, 1962, *78*, 544–552.
15. Miller, C. E. Experimental evaluation of multiple-crystal arrays and single-crystal techniques. Symposium on Whole Body Counting, IAEA, Vienna, 1962, pp. 81–120.
16. Norris, W. P., Speckman, T. W., and Gustafson, P. F. Studies of metabolism of radium in man. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1955, *73*, 785–802.

17. Norris, W. P., Tyler, S. A., and Brues, A. M. Retention of radioactive bone-seekers: calculations based on power function cast doubt on present concept of biological half-times. *Science*, 1958, *128*, 456–462.
18. Rowland, R. E. Resorption and bone physiology. To be published.
19. Rowland, R. E. Some aspects of human bone metabolism deduced from studies of radium cases. To be published.
20. Rowland, R. E., and Marshall, J. H. Radium in human bone: dose in microscopic volumes of bone. *Radiation Res.*, 1959, *11*, 299–313.
21. Rowland, R. E., Marshall, J. H., and Jowsey, J. Radium in human bones: microradiographic appearance. *Radiation Res.*, 1959, *10*, 323–334.
22. Spiers, F. W., and Busch, P. R. J. Measurements of body radioactivity in radium worker. *Brit. J. Radiol.*, 1957, 81–89. Supplement 7.
23. Stehney, A. F., and Wallace, D. E. Dibutyl phosphate as extractant of radiothorium from bone. *Radiation Res.*, 1956, *5*, 598.
24. Wallace, D. E., Stehney, A. F., and Ilcewicz, F. H. Calibration of dibutyl phosphate procedure for isolation of Th^{228} from bone. Argonne National Laboratory Radiological Physics Division Semiannual Report, January-June, 1957, ANL-5755, 33.

◆

THE USE OF IODINE 125 IN THYROID SCINTISCANNING*

By N. DAVID CHARKES, M.D., *and* DAVID M. SKLAROFF, M.D.
with the technical assistance of Mrs. Tina Helock and Miss Barbara Cravitz
PHILADELPHIA, PENNSYLVANIA

THE use of iodine 125 for thyroid scintiscanning has been advocated because its unique physical properties may provide superior scans with less radiation dosage to the patient as well as greater safety in handling, in comparison with iodine 131.[2,8]

I^{125} decays by electron capture to stable tellurium 125, the principal radiation being the 27.4 kev. K_α roentgen ray of Te^{125}, which is emitted twice in 80 per cent of the disintegrations of I^{125}. A 35.4 kev. unconverted gamma ray emerges in 7 per cent of the disintegrations as well, making a total of 1.43 "usable" photons emitted per decay after correction for internal conversion.[8] These soft roentgen and gamma rays are more easily collimated than are the more energetic gamma rays of I^{131} with existing commercial collimators, thereby sharpening resolution. "Cold" nodules might appear colder with I^{125} than with I^{131} since I^{125} radiations emerging from tissue posterior to the nodule are more readily absorbed by the nodule and soft tissues of the neck than are the I^{131} gamma rays. This is so because the thickness of a water phantom (6.3 cm.) which transmits 50 per cent of the 364 kev. gamma rays of I^{131} passes only 14 per cent of the I^{125} gamma rays.[8] The increase in resolution with I^{125} should permit detection of nodules considerably smaller in size than are now detectable with I^{131}.[2] Endlich *et al.*[2] and Levy and associates[7] have demonstrated that these considerations are probably valid since I^{125} thyroid scintigrams appear to be equivalent to, and in some cases superior to, those obtained with I^{131}.

Although the half life of I^{125}, 60 days, results in more prolonged radiation to the thyroid gland, its increased shelf life offers another advantage to the user. Its cost at present is considerably greater than that of I^{131}, although improved manufacturing processes could make it competitive.[2,8]

To date we have scanned the thyroid glands of 97 patients with I^{125}, and in 20 of these we have obtained I^{131} scans as well. Our findings indicate that in most cases there appears to be little difference between these isotopes although in certain instances where increased resolution is required, as in depicting some cold nodules or small pyramidal lobes, I^{125} is superior. On the other hand, I^{131} scans of substernal goiters were found to be more accurate.

METHODS

The equipment employed was the Picker Magnascanner, which utilizes a 3×2 inch sodium iodide (Tl) crystal, pulse-height analyzer, and 31 hole focusing collimator. The device was not modified for use with I^{125}. All patients received a dose of I^{125} which was calculated to produce a count rate of 1,500 to 2,000 counts per minute when the focusing collimator was placed 7.5 cm. over the hottest portion of the thyroid gland 24 hours later. This dose usually amounted to 50 to 100 μc, although less was used in some hyperthyroid patients. In 20 patients an equivalent dose of I^{131} was given at the completion of the I^{125} scan and the scintigram was repeated in 24 hours, the I^{125} energies being screened out by the pulse-height analyzer.

In peaking the Magnascanner for the I^{125} scintigram, it was found expedient to vary the high voltage, with a fixed gain of 9.0,

---

* From the Department of Radiology (Divisions of Nuclear Medicine and Radiation Therapy), Albert Einstein Medical Center, Northern Division, Philadelphia, Pennsylvania.

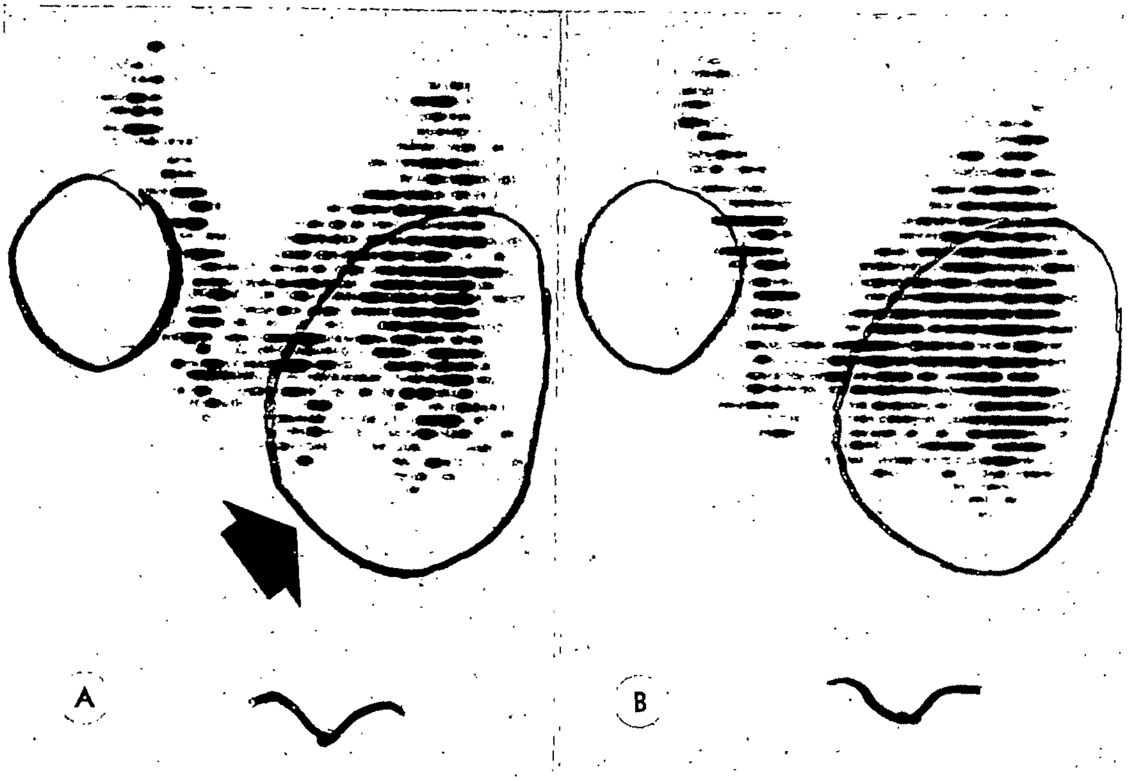


Fig. 1. (J.O.) Uptake 14 per cent in 24 hours. (*A*) I^{125} scan, 100 μc. Arrow points to poorly functioning nodule. The radioiodine in this area is inhomogeneously dispersed. (*B*) I^{131} scan, 100 μc, settings same as in *A*. Iodine uptake appears more uniform in nodule. Operative findings revealed bilateral follicular adenomata

utilizing an I^{125} source and a narrow window straddling 300 pulse-height units. If too little high voltage is applied or if the gain is too low, interfering electronic noise creates serious artifacts on the photoscan. A helipot setting of approximately 740 to 820 hv units was found satisfactory (0 to 1,000 scale). After the scanner was peaked, the window was opened to straddle the photopeak; settings of 210 to 380 pulse-height units were found to be convenient for this purpose. The count range differential was set at 80 per cent for each scan (*i.e.*, background cutoff for the photoscan was 20 per cent, with contrast enhancement of the remaining pulses).[6] A scan speed of 16–18 cm./minute was used. The dial settings for the I^{131} scans were identical to the I^{125} scans so that direct comparisons could be made.

RESULTS

Ninety-seven patients were scanned with I^{125}, and in 20 patients I^{131} scans were also obtained. A wide variety of thyroid disorders was studied, including diffuse toxic goiter (9 cases), thyroid carcinoma (2 cases), multinodular nontoxic goiters (17 cases), and nontoxic uninodular glands containing hyperfunctioning (1), normally functioning (10), and nonfunctioning nodules (18), as well as 23 patients in whom no thyroid disease was found.

In general, the scans were comparable. However, in some instances the I^{125} scan proved superior, particularly in delineation of some poorly functioning nodules (Fig. 1, *A* and *B*) and pyramidal lobes (Fig. 2, *A* and *B*). A cold nodule 0.9 cm. in diameter, confirmed by excisional biopsy, was successfully identified.

There were only 2 scans with I^{125} which were felt to be unreliable, and these involved substernal extensions of the thyroid gland. In both cases I^{131} scans were also performed for comparison. In the first of these 2 patients (Fig. 3, *A* and *B*), the I^{131} scan provided a clue to the presence of a substernal adenoma, in the form of a curvilinear tongue of thyroid tissue which extended into the superior mediastinum and outlined a portion of the nodule. The I^{125} scan did not delineate this functioning capsule as well, and the adenoma might have been missed without the I^{131} scan. In the second patient (Fig. 4, *A* and *B*) with a 5×5 cm. substernal goiter, the I^{131} scan gave a truer picture of the extent of the lesion and its function than did the I^{125} scan.

Fourteen of the 97 patients underwent operative procedures on the thyroid gland and in 12 of these patients sufficient pathologic data concerning the size of nodules were available for evaluation of the photoscan findings (Table 1). It is evident that the I^{125} photoscan approximated the true nodule size although there was a tendency to overestimate the actual dimensions.

The maximum count rate over the thyroid gland 24 hours after the administration of I^{125} with the 31 hole focusing collimator was 70 to 300 cpm./μc deposited in the gland, with a mean of 147 cpm./μc ± 55 (1 S.D.).

DISCUSSION

The results of this study of 97 patients confirm the work of Endlich *et al.*[2] and Levy *et al.*[7] that I^{125} appears to be equivalent to, and in some cases superior to, I^{131} for thyroid scintiscanning. The soft roentgen rays emerging from the I^{125} decay process result in improved collimation and increased resolution so that cold nodules smaller than 1 cm. in diameter have been unequivocally depicted, and small pyramidal lobes have been identified that in the past were probably missed with I^{131}. Except for substernal goiters, in no patients were I^{131} scans superior to I^{125} scans.

In order to evaluate resolution under controlled conditions, a phantom was scanned which contained voids of 0.6 cm., 1.0 cm., and 1.3 cm. in diameter in a lucite block filled with 35 ml. of sodium iodide solution in the shape of a thyroid gland.[3] I^{131} and I^{125} solutions were tested in concentrations which could be found in a human thyroid. Scan and dial settings were

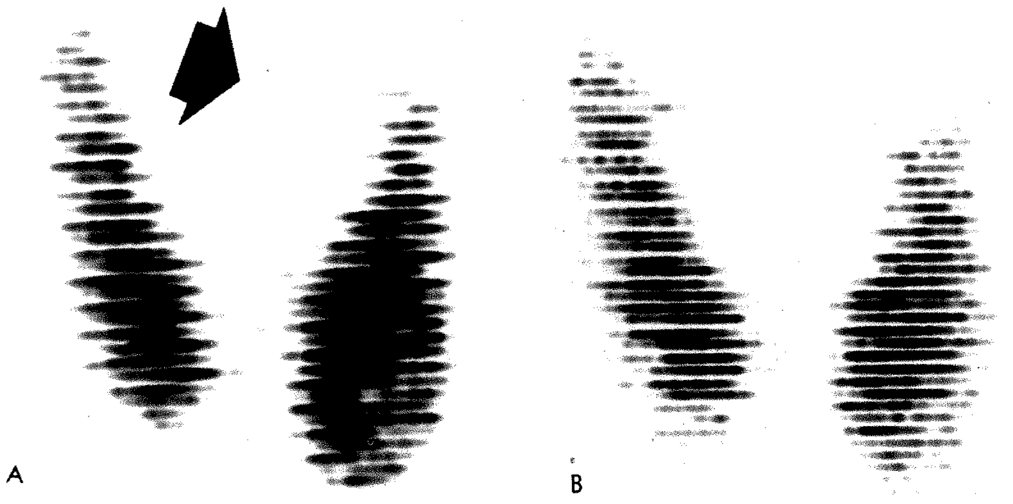


FIG. 2. (S.P.) Diffuse toxic goiter. Uptake 54 per cent in 24 hours. (*A*) I^{125} scan, 30 μc. Arrow points to pyramidal lobe. (*B*) I^{131} scan, 30 μc, settings same as in *A*. Pyramidal lobe is very faint.

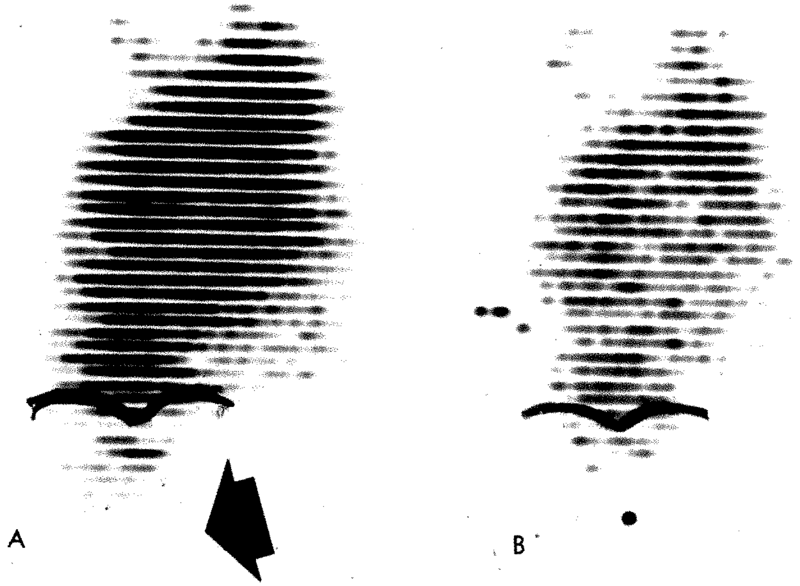


Fig. 3. (M.B.) Hürthle cell carcinoma of thyroid and previous right lobectomy for diffuse toxic goiter. (*A*) I^{131} scan, 100 μc. Arrow points to curvilinear tongue of functioning tissue extending into retrosternal space and outlining a "cold" nodule. (*B*) I^{125} scan, 100 μc, settings same as in *A*. Retrosternal extension poorly visualized and nodule would have been missed. Operative findings revealed colloid adenoma.

comparable to those used clinically, including range differential of 80 per cent (20 per cent background photo-cutoff). Under these conditions it was not possible to demonstrate any perceptible differences between the two isotopes in depicting small cold lesions.

In all cases in which both I^{125} and I^{131} were used in equivalent dosage for scanning, the I^{125} scan was performed first, since the softer I^{125} photons were easily screened out by a discriminator. It was possible to perform simultaneous I^{125} scintigrams with 50 to 100 μc and uptake studies with 12 μc of I^{131}, either by utilizing a lower level discriminator or by decreasing the input sensitivity of the scaler so that no I^{125} pulses were passed. It was found that I^{131} gave only 6 per cent of the counts at the I^{125} setting of the scanner as compared to the I^{131} setting, and since the count rates per microcurie in the gland for each isotope at its own setting were approximately the same, a 12 μc uptake dose of I^{131} contributed an additional count rate of less than 1 per cent to that of 100 μc of I^{125}. From these considerations it is apparent that simultaneous radioiodine uptake studies with I^{131} in small amounts and thyroid scintigrams with I^{125} in doses of 50 to 100 μc are permissible under the conditions noted. Thyroidal uptake with I^{125} is not considered reliable at present because of high tissue absorption.[7]

It is to be emphasized that in these studies no modification of existing equipment for use with I^{125} was undertaken. The aluminum can housing the sodium iodide crystal in the detector is thick enough to attenuate about 40 per cent of the I^{125} roentgen rays incident upon it.[2] By utilizing crystals with thin aluminum windows such as described by Myers and Vanderleeden,[8] it should be possible to increase detection efficiency almost twofold and thereby permit a significant reduction in dose to the patient.

In 2 patients with substernal extensions of the thyroid gland, the I^{131} scan was superior to the I^{125} scan. A consideration of the relative absorption of the principal photons by bone shows why this is so. Bone absorbs 460 ergs/gm./roentgen of the 27.4 kev. roentgen ray of I^{125} but only 86.5 ergs/gm./roentgen of the 364 kev. I^{131} gamma ray, a 5.3-fold increment.[4] Thus, to make an I^{125} scan of a substernal goiter comparable to I^{131}, a dose of up to five times the usual would have to be administered, depending upon the thickness of the overlying bone. Since the thyroidal dose from I^{125} is 84 per cent that of I^{131},* the integral dose to the gland from a five-fold larger I^{125} dose would be (0.84×5.0) or 4 times that of one-fifth the amount of I^{131}. The slightly greater amount of information possibly obtainable from I^{125} scanning does not warrant this excessive dosage, and furthermore, scattering of roentgen rays by bone could offset the increase in resolution obtainable in soft tissue studies.

Because I^{125} scans of substernal goiters are misleading and unreliable as a result of excessive photon attenuation by overlying bone, the isotope is not suitable for this type of study.

Another use for I^{125} scanning, mentioned by Levy *et al.*[7] is in conjunction with I^{131} in stimulation and suppression tests of thyroid function. The I^{125} scan is performed first, followed by TSH or L-triiodothyronine. The gland is then scanned with I^{131}, the soft photons of the first isotope being screened out by the pulse-height analyzer. Under these circumstances, it was possible to evaluate the influence of TSH on poorly functioning tissue and of L-triiodothyronine on functioning nodules. Without the use of two isotopes, such a study would

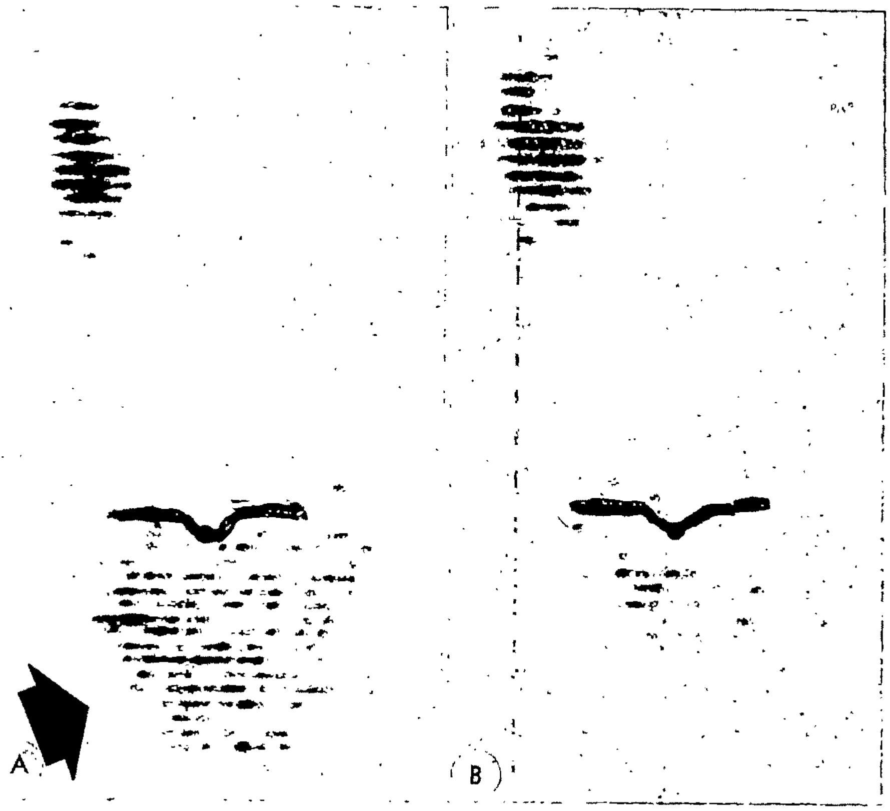


Fig. 4. (H.K.) Previous left lobectomy for adenoma. (*A*) I^{131} scan, 100 μc. Arrow points to retrosternal goiter displacing trachea to right. (*B*) I^{125} scan, 100 μc, settings same as in *A*. Volume of goiter is apparently less, due to attenuation of soft roentgen rays by overlying bone. Note right lobe of equal density on both scans.

---

* See Appendix.

TABLE I

CORRELATION OF NODULE SIZE ON PHOTOSCAN WITH PATHOLOGIC FINDINGS

Patient	Nodular Size (cm.)		Photoscan Function	Histopathology
	Photoscan	Biopsy		
L.S.	2.1	2.0	Cold	Follicular adenoma
S.S.	1.1 2.1	1.2 2.4	Cold Cold	Follicular adenoma Follicular adenoma
A.B.	2.6×2.0	2.0×1.5	Cold	Follicular adenoma
A.N.	1.3×1.2	1.0×0.8	Cold	Cystic degeneration
J.O.	5.0×3.3	4.5×3.5	Warm	Follicular adenoma
D.G.	1.4	0.8	Cold	Follicular carcinoma
P.H.	5.0	4.2	Cold	Follicular adenoma
L.St.	2.4	2.0	Warm	Follicular adenoma
G.G.	2.2	2.0	Cold	Nodular colloid goiter
D.C.	3.5	3.0	Cold	Microfollicular adenoma
P.O.	0.8	0.9	Cold	Follicular adenoma
W.S.	2.9	3.2	Warm	Nodular colloid goiter

have to be prolonged over several weeks or months to allow sufficient time for the I^{131} initially present to decay.[5]

In 16 patients a midline extension of the thyroid gland, identifiable as a pyramidal lobe, was demonstrated. Eight of these 16 patients either had diffuse toxic goiter at the time of study or had been surgically treated for this disease in the past. Of the remaining 8 patients, 4 had nodular glands and 4 had no demonstrable thyroid disorder. Thus, in 75 per cent of cases (12 of 16), the presence of a pyramidal lobe signified localized or generalized hyperplasia of the thyroid gland either at the time of study or in the past. However, midline functional ectopic thyroid tissue was found in 4 of our 23 patients with presumably normal thyroid glands, an incidence of 17 per cent. A detailed evaluation of these data will be presented elsewhere.[1] In 5 of the 16 patients I^{131} scans were also obtained which in general were inferior to the I^{125} scans (Fig. 2, *A* and *B*). The increased resolution obtainable with I^{125} proved to be of real value in identifying and depicting the frequently faint pyramidal lobe.

The dosage to the thyroid gland from an I^{125} scan is approximately 4.8 rads per μc deposited in the gland (see Appendix). The dose to an adult thyroid gland which would produce a satisfactory count rate for photoscanning would be about 145 rads, assuming an uptake of 30 per cent and 100 μc administered. A comparable dose of I^{131} would yield approximately 172 rads.

SUMMARY

Thyroid scintiscanning was performed in 97 patients with iodine 125, and in 20 of these patients I^{131} scans were also done, utilizing unmodified conventional photoscanning equipment.

In general, I^{125} scans were comparable in quality to those produced by I^{131}. In circumstances in which high resolution was

required, as in defining some cold nodules or small pyramidal lobes, I^{125} proved superior. I^{125} scans of substernal goiters were inferior to those produced by I^{131}.

I^{125} thyroid scintigrams may be made simultaneously with I^{131} uptake studies and in conjunction with I^{131} in stimulation and suppression tests of thyroid function.

N. David Charkes, M.D.
Department of Radiology
Albert Einstein Medical Center
York and Tabor Roads
Philadelphia 41, Pennsylvania

REFERENCES

1. Charkes, N. D., and Sklaroff, D. M. Surgical significance of thyroidal pyramidal lobe. To be published.
2. Endlich, H., Harper, P., Beck, R., Siemens, W., and Lathrop, K. Use of I^{125} to increase isotope scanning resolution. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *87*, 148–155.
3. Endlich, H. L. Some modifications of photoscanning techniques. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *87*, 156–160.
4. Glasser, O. Medical Physics. Vol. II. Year Book Publishers, Chicago, 1944, p. 791.
5. Górowski, T., and Chomicki, O. Diagnosis of nontoxic "warm" thyroid nodules independent of TSH. *J. Clin. Endocrinol. & Metabol.*, 1962, *22*, 1267–1268.
6. Herring, C. E. Universal photorecording system for radioisotope area scanners. *J. Nuclear Med.*, 1960, *1*, 83–101.
7. Levy, L. M., Estrellado, T. T., Okezie, O., and Stern, H. S. Use of I^{125} in clinical nuclear medicine. *J. Nuclear Med.*, 1962, *3*, 183–184 (abstract).
8. Myers, W. G., and Vanderleeden, J. C. Radioiodine-125. *J. Nuclear Med.*, 1960, *1*, 149–164.
9. Report of Committee II on Permissible Dose for Internal Radiation. Recommendations of the International Commission on Radiological Protection, Publication #2, Pergamon Press, New York, 1959, p. 193.

APPENDIX

The integral thyroidal dose per μc deposited is given by:

$$D_{\beta+\gamma} = \{(73.8\bar{E}_\beta) + (0.0346)\Gamma g\} \cdot \text{eff. } T\tfrac{1}{2} \cdot C$$

where

	I^{131}	I^{125}	units
$\bar{E}_\beta$	0.187	0.021[2]	mev.
Γ	2.18	1.30	r/mc/hr. @ 1 cm.
g	17	17	geometry factor
eff. $T\frac{1}{2}$	7.6	42	days
C	0.05	0.05	μc/gm.

assuming a biologic half-life of 138 days and a thyroidal weight of 20 grams.[9]

$\therefore$ I^{131} dose = 5.7 rad/μc deposited.
I^{125} dose = 4.8 rad/μc deposited.

FECAL EXCRETION OF I^{131}

A PITFALL IN INTERPRETATION OF BODY SCANS

By BERNARD SCHENCKER, CAPT., M.C., U.S.A.,* *and* JOSEPH L. MARCARELLI, MAJOR, M.C., U.S.A.†
FORT SAM HOUSTON, TEXAS

WHOLE body scanning after I^{131} administration for evaluation of possible metastatic thyroid carcinoma is a well accepted and useful procedure.[5] Manual scanning, using an easily movable, well collimated, scintillation probe, is rapidly performed 24–72 hours after oral administration of I^{131}. Areas of increased concentration may then be better defined and documented by automatic scanning. This method provides a sensitive means for early detection of thyroid metastases.[2,4]

Increased activity due to concentration of I^{131} in the heart, liver, spleen, stomach, kidneys, and bladder does occur and must not be mistaken for evidence of metastatic deposit.[5,7] Fortunately, these concentrations are more marked during the early hours after I^{131} administration, and are rarely bothersome when scanning is done at 72 hours. Of course, an empty bladder greatly facilitates interpretation in the pelvic area.

Recently, using a 72 hour technique, we have become aware of another pitfall in diagnosis, which to our knowledge has not been previously emphasized. Increased activity over the abdomen and pelvis has been found to be due to accumulation and concentration of I^{131} in fecal material within the colon. Early in our experience, before this source of activity was understood, these I^{131} concentrations were of great concern. In fact, one patient was treated for nonexistent metastases because of our ignorance of this phenomenon. This case serves to illustrate the problem.

REPORT OF A CASE

Mrs. R.J., a 38 year old female, had follicular and papillary adenocarcinoma of the thyroid gland, treated by surgery and I^{131} ablation. This therapy was completed in August, 1959. The patient was maintained on 3 grains of desiccated thyroid daily. Follow-up cervical and whole body scans in October 1959, April 1960, and May 1961 were negative.

In October, 1961 manual and automatic scanning of the abdomen revealed increased activity over the left ilium and sacrum (Fig. 1*A*). Ten days later repeat tracer studies were obtained. At this time the automatic scan corroborated activity over the sacrum, but not over the ilium (Fig. 1*B*). However, some increased activity was detected over the ilium on a manual scan and uptake over the left iliac wing was 50 per cent greater than that obtained over the right ilium; even as long as 5 days after I^{131} administration. Seventy-two hour urinary excretion was 97.3 per cent, and uptake over the neck was 0.1 per cent. The patient had been complaining of low back and left iliac pain. Complete bone survey and chest roentgenograms were negative.

Although scan findings were confusing, it was felt that (on the basis of prolonged activity detected on manual scan) the patient had metastasis of the sacrum and left iliac wing. A visiting consultant concurred, and the patient was given a therapy dose of 92 mc of I^{131}.

In January, 1962 a follow-up tracer study was negative. The examiner, however, did note some increased activity over the pelvis, which was ascribed to concentration of I^{131} in the bladder and felt to be of no significance. Only manual scanning was performed.

In July, 1962, one month after discontinuation of thyroid medication, the patient received the usual tracer dose of 1.0 mc of I^{131}. Manual and automatic body scans, at this time, revealed definite increased activity over the lower abdomen (Fig. 2*A*). The pattern closely resembled the contour and course of the lower

---

* Resident in Radiology, Brooke General Hospital, Ft. Sam Houston, Texas.

† Chief, Radioisotope Clinic, Brooke General Hospital, Ft. Sam Houston, Texas.

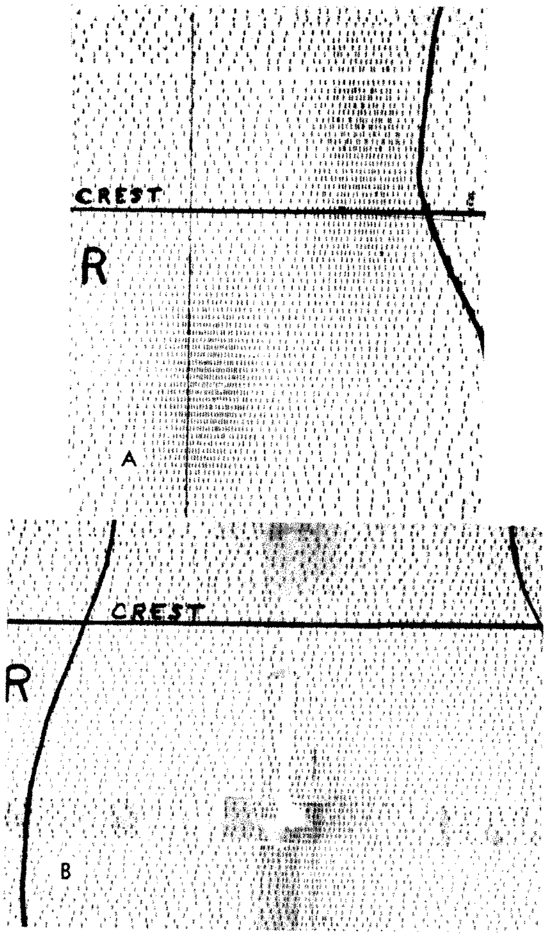


Fig. 1. (*A*) Automatic body scan in October, 1961 demonstrating increased activity over sacrum and left side of abdomen. (Crest = level of iliac crest.) (*B*) Same patient 10 days later after second tracer dose. Increased activity only over sacrum. Incorrect interpretation of these scans and persistence of activity over left iliac crest on repeated manual scans led to treatment for presumed bony metastases.

descending and sigmoid portions of the colon. A barium swallow study ruled out a low lying stomach, and an abdominal roentgenogram demonstrated fecal material in the descending and sigmoid colon corresponding to the configuration of activity found on the scan (Fig. 2*B*). An enema was then administered and the abdomen rescanned. As anticipated, the activity over the left lower abdomen was no longer detected (Fig. 2*C*). A sample of excreted feces was found to contain definite activity. A repeat abdominal roentgenogram now showed the lower colon to be free of fecal material (Fig. 2*D*). It was therefore obvious that the activity was due to fecal concentration rather than metastatic deposit.

With this recent scan in mind, the scans of October and November, 1961 were carefully reviewed. The configuration on the October scan coincided with that of the colon, with activity actually extending well above the iliac crest (Fig. 1*A*). The November scan probably was due to residual activity in the rectum (Fig. 1*B*). In retrospect, then, it would seem that fecal concentration of I^{131} was in fact responsible for activity detected over the ilium and sacrum. Bony metastases were not present and the patient was therefore unnecessarily treated.

DISCUSSION

Fecal excretion of iodine is not well defined.[6] It is generally felt that oral

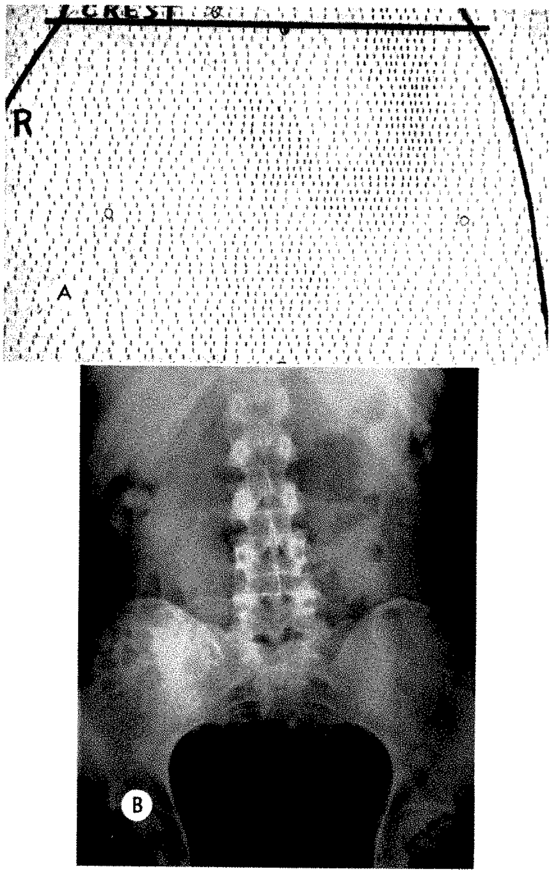


Fig. 2. (*A*) Body scan in July, 1962 demonstrating increased activity over left lower abdomen and pelvis. (*B*) Abdominal roentgenogram after scan showing fecal material in lower descending colon and sigmoid corresponding to configuration on scan.

iodides are rapidly and completely absorbed from the gastrointestinal tract, and that fecal excretion of inorganic iodide is negligible.[1,3,6] Organic iodine, incorporated in thyroid hormone, does, however, find its way into the colon in significant amounts. Approximaetly 10–15 per cent of iodine from degraded thyroid hormone is excreted in the feces daily.[1,6] This excretion is not ordinarily found until the third day after an oral iodide dose, presumably because of the time necessary for organification and release of thyroid hormone from the thyroid gland. Of course, these measurements are made on excreted feces and scanning of the colon might be expected to reveal significant activity at an earlier time.

Since our patients are athyrotic, having had total thyroid ablation, fecal excretion of organic iodine is not expected. One then wonders why significant I^{131} activity is found in the colon in these subjects. At first it seems reasonable to postulate altered physiology and possibly decreased gastrointestinal absorption of orally administered iodide as an explanation. The answer, however, seems to us to be much simpler. Our patients receive a 1.0 mc dose. If even only a "negligible" amount, 1 per cent (10 μc) is excreted into the gut and this then concentrated into a relatively small volume of fecal matter by constipation, a significant scan is easily obtained. Since our patients are hypothyroid* at the time of study and almost always constipated, this phenomenon is not unexpected. On the other hand, a euthyroid patient given a small tracer

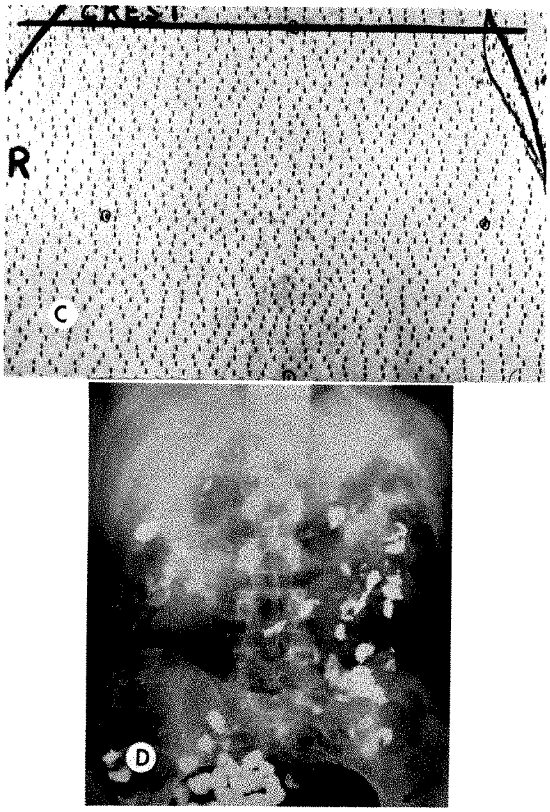


Fig. 2. (*C*) Repeat scan after enema. No evidence of increased activity. (*D*) Abdominal roentgenogram after enema showing absence of fecal material in lower colon corresponding to negative scan.

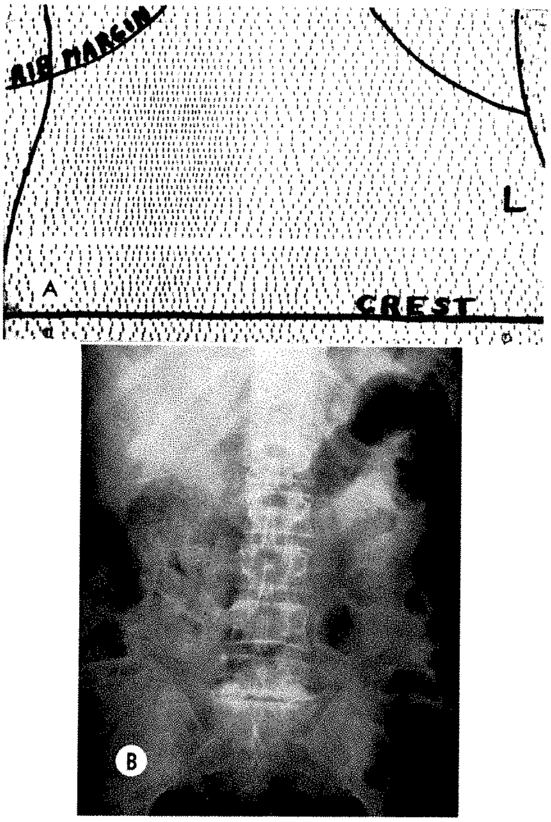


Fig. 3. (*A*) Demonstration of fecal concentration in right colon. Increased activity in right upper abdomen. (*B*) Abdominal roentgenogram taken shortly after scan showing large amount of fecal material in ascending and hepatic flexure areas of colon. Note close correlation with scan.

---

* Desiccated thyroid is discontinued 4 weeks prior to testing. In some cases the patients are placed on cytomel, which is then discontinued 1 week prior to evaluation.

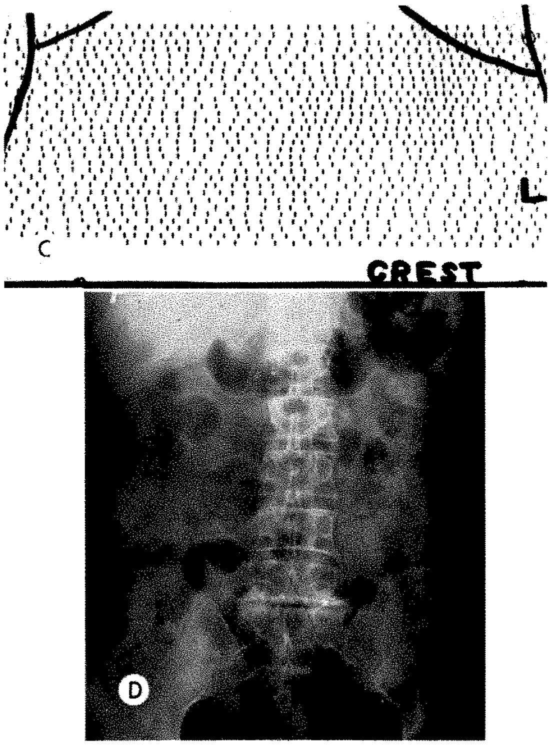


FIG. 3. (*C*) Scan after enema. Note absence of activity on right. Small area of increased activity now present beneath left costal margin. (*D*) Abdominal roentgenogram after enema showing absence of feces on right with small amount now present in area of splenic flexure corresponding to *C*.

dose would probably not concentrate enough in the colon to be detected by ordinary techniques; accounting for the general unawareness of this process.

Regardless of the basis for it, fecal concentration of I^{131} does occur in patients being evaluated for thyroid metastases. This concentration is often large enough to be detected by manual and automatic scanning techniques. Although in most cases increased activity is found over the lower descending and sigmoid areas of the colon, it may be discovered over any portion of the large bowel (see Fig. 3, *A–D*). If significant activity is discovered over the abdomen on a manual scan, an enema followed by rescanning often solves the problem. Comparison of an automatic scan with an abdominal roentgenogram may also be helpful in outlining the colon as the source of activity. On occasion, lateral scanning may be useful in ruling out a true bony lesion. Once considered and defined, fecal concentration should cause no real problem in scan interpretation. Misdiagnosis and mistreatment should not occur.

SUMMARY

1. Whole body scanning after oral I^{131} is a useful and generally accepted procedure for detection of metastatic thyroid disease.

2. Problems in scan interpretation due to concentration of I^{131} in certain organs are well known.

3. A new pitfall—fecal concentration of I^{131}—leading to misdiagnosis is reported and discussed.

Bernard Schenker, Capt., M.C., U.S.A.
Chief, Department of Radiology
U. S. Army Hospital
Fort Jackson, South Carolina

REFERENCES

1. BERSON, S. A., and YALOW, R. S. Quantitative aspects of iodine metabolism. *J. Clin. Invest.*, 1954, *33*, 1533–1552.
2. CATZ, B., and STARR, P. Cancer of thyroid, with metastases to lungs; condition shown by scintigram in absence of definite x-ray findings. *J.A.M.A.*, 1956, *160*, 1046–1047.
3. KEATING, R. F., POWER, M. H., BERKSON, J., and HAINES, S. F. Urinary excretion of radioiodine in various thyroid states. *J. Clin. Invest.*, 1947, *26*, 1138–1151.
4. KRAMER, S., CONCANNON, J. P., and CLARK, G. M. Thyroid carcinoma; report on diagnostic and therapeutic use of radio-iodine. *Brit. J. Radiol.*, 1955, *28*, 307–313.
5. QUIMBY, E. H., FEITELBERG, S., and SILVER, S. Radioactive Isotopes in Clinical Practice. Lea & Febiger, Philadelphia, 1958, pp. 342–343.
6. RIGGS, D. S. Quantitative aspects of iodine metabolism in man. *Pharmacol. Rev.*, 1952, *4*, 284–370.
7. SONENBERG, M., and RALL, J. E. Use of radioactive iodine in carcinoma of thyroid. *M. Clin. North America*, 1956, *40*, 821–833.

LIVER SCANNING FOR EXTRAHEPATIC TUMORS*

By T. A. O'DONNELL, M.B.†
PITTSBURGH, PENNSYLVANIA

A DEFECT or "cold" area in the liver scintiscan is usually attributed to an intrahepatic lesion which does not absorb the administered radioactive compound. In this paper "cold" areas due to extrahepatic tumors which indent and distort the liver scan pattern are described. The anatomic relationship of an extrahepatic abdominal tumor to the liver can be clearly shown when a normal liver scan distinct from the tumor is obtained. However, when a "cold" area continuous with an abdominal tumor extends into the liver scan pattern it may be difficult to decide whether (1) the tumor originates in the liver and is extending into the abdominal cavity or (2) the tumor is extrahepatic and its growth expansion displaces a portion of the liver, thus producing a corresponding defect on the scan.

In the case reported and also in one discussed the latter proved to be the correct explanation. Figure 1*A* is an Au^{198} anterior liver scan superimposed on a roentgenogram of the abdomen. This was interpreted as "gross enlargement of the liver, particularly of the left lobe, with replacement of the major portion of the right lobe by an intrahepatic mass." At autopsy a huge tumor of the right adrenal gland was found to occupy most of the right upper quadrant of the abdomen. In retrospect, the correct reading of the scans should have been "displacement of the liver to the left, and thinning of the liver tissue which lies anterior to a right upper quadrant tumor."

Figure 1*B* is the diagrammatic interpretation of the scan shown in Figure 1*A*. It depicts the defect corresponding to the position of the tumor and the diminished area of activity corresponding to the wedged or thinned segment of the right lobe. The posterior scan (Fig. 2) shows all the activity to be to the left of the midline. This is in keeping with the findings of the anterior scan where the major activity was also on the left. The small amount of radioactivity from the right lobe is not detected on this scan as the tumor mass shields it from the detector.

REPORT OF A CASE

On her admission to the hospital, K.C., a 60 year old Negro female, had right subcostal pain as her chief complaint. The patient had been in good health for her entire life until approximately 5 months before her admission when she developed an episode of "flu" and right-sided pneumonia, for which she was treated by her family physician at home. From this time on she experienced right subcostal pain, and pain in the right upper quadrant and right flank occurring intermittently each day and lasting for varying periods from minutes to hours but relieved by analgesics. Fever or chills did not accompany the pain. Previous surgical operations included the removal of a goiter in 1926 and a hysterectomy for fibroids in 1937.

On physical examination she was found to be well-developed; her blood pressure was 115 systolic and 70 diastolic, the pulse was regular at 96 per minute, respirations 22 per minute and temperature 98°F. The lungs were clear to auscultation and percussion but the right diaphragm was found to be elevated and fixed. Examination of the heart was normal. The abdomen was protuberant and a mass was palpable five finger breadths below the right costal margin; this was assumed to be the liver edge. On percussion the upper border of the liver reached the third intercostal space on the right. The spleen or kidneys were not palpable; pelvic and rectal examinations were negative. No significant enlargement of the lymph nodes was found.

Laboratory data were as follows: hemoglobin 7.5 gm., hematocrit 24 per cent, white blood cell count 7,600 per ml., and the differential count was 61 per cent polymorphonuclear leukocytes, 34 per cent lymphocytes and 4 per

---

* From the Department of Radiation Therapy, The Presbyterian-University Hospital, Pittsburgh, Pennsylvania.

† Assistant Professor of Radiology, University of Pittsburgh, Pittsburgh, Pennsylvania.

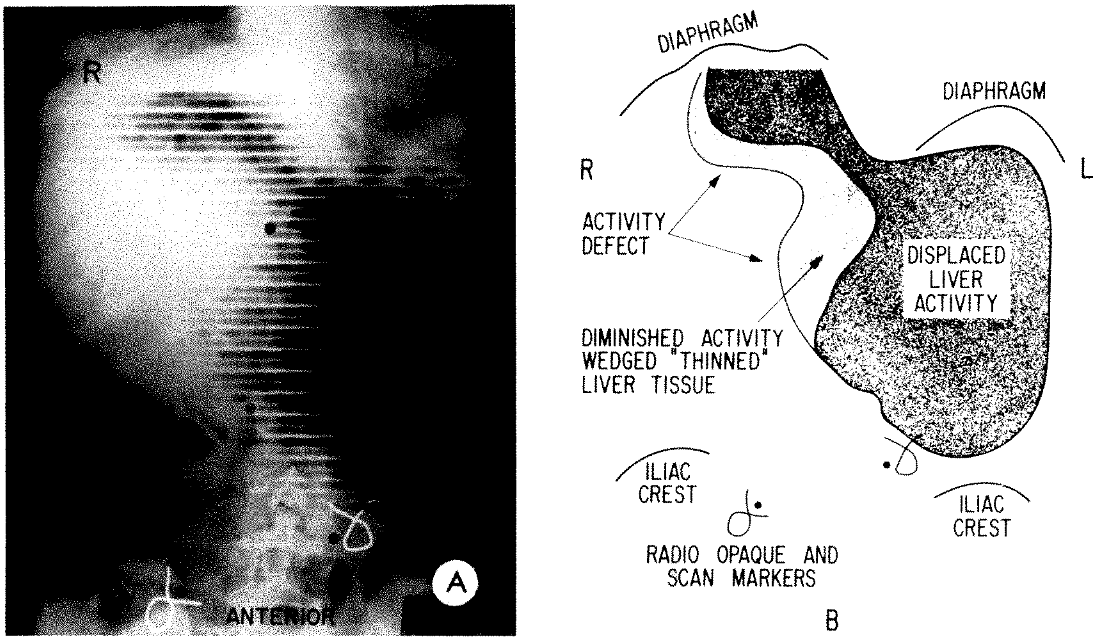


FIG. 1. K.C. (*A*) Au^{198} anterior liver photoscan superimposed on a roentgenogram of the lower chest and abdomen. (*B*) Diagrammatic interpretation of *A* showing the position of the diaphragm and iliac crests.

cent monocytes. The red blood cells were normochromic and normocytic on blood smear.

Two units of whole blood were administered to the patient and the hematocrit increased to 31 per cent and the hemoglobin to 9.7 gm. Blood chemical estimations showed: bromsulphalein 2 per cent; alkaline phosphatase 9.2 units; total proteins 9 gm. with increased globulin and decreased albumin; cephalin-cholesterol flocculation 2+, thymol turbidity 1+, bilirubin 0.3 mg./100 ml. total with 0.1 mg./100 ml. direct; and a sedimentation rate of 41 mm. Serology showed 3+ reactive VDRL. Urinalysis was negative. Ascaris was found in the feces in one of three examinations but no amebae were noted; the guaiac test was repeatedly negative.

The chest roentgenogram showed the right hemidiaphragm to be elevated with displacement of the cardiac shadow to the left. The upper gastrointestinal series revealed displacement of the stomach and liver.

Liver biopsy was attempted, fluid was obtained and air was injected. On roentgenograms several levels suggestive of fluid and air in separate pockets were demonstrated beneath the right hemidiaphragm. A diagnosis of subdiaphragmatic amebic abscess was made and the patient was placed on chloroquine, 250 mg., and tetracycline, 500 mg., four times a day.

Liver scans were then obtained (Fig. 1*A* and 2) following the intravenous injection of 250 μc of Au^{198}. It was felt that these confirmed the diagnosis of an amebic abscess and were helpful in carrying out further aspiration and introduction of contrast material. On serial roentgenograms the size of the abscess was seen to be diminishing. Blood transfusions were administered in order to make up the hemoglobin loss from the cyst fluid.

During the beginning of the third month after admission to hospital, the patient's temperature rose above 100°F. and blood and urine

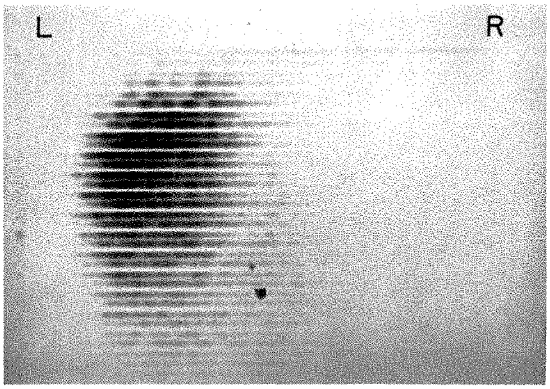


FIG. 2. K.C. Au^{198} posterior liver scan showing that the radioactivity is to the left of the midline.

cultures showed tetracycline resistant *E. coli.* The cyst fluid was also found to be infected with *E. coli* and *Proteus vulgaris.* Streptomycin and chloromycetin were administered for this infection; however, the latter drug was discontinued after 7 days. The cyst continued to be secondarily infected with *Proteus* and *E. coli* and eventually hemolytic *Streptococci.* In the last few days of life, the patient's temperature rarely fell below 100°F. and at termination it rose to 103°F. She died approximately 4 months after her admission to hospital and 9 months after the onset of symptoms. Roentgenograms of the thorax and abdomen during the course of her illness all had shown an elevated right diaphragm and compression of the right lower lung with deviation of the heart to the left.

At autopsy, a huge retroperitoneal mass was found below the liver on the right side of the abdomen, causing a deviation of the abdominal organs to the left. The vault of the diaphragm was elevated to the second interspace on the right and third interspace on the left. The anterior liver margin was 2 cm. below the costal margin at the mid-clavicular line and 3.5 cm. below the xiphoid process. The right lobe of the liver was compressed and seemed to be unusually soft and friable. Numerous fibrous adhesions connected its lower aspect to the tumor mass. The liver itself was found to be normal in size and weight and on section the normal architecture was present. Approximately 2.5 cm. of the right lobe was wedged between the tumor mass and the diaphragm.

A huge tumor (Fig. 3) which measured 25 cm. in its greatest dimension was found attached to the right kidney and in the region of their attachment they shared a thick fibrous capsule. The tumor could be separated from the superior pole of the right kidney and the right kidney itself was normal. There was thickening of Bowman's capsule on PAS staining and patchy infiltration by mononuclear cells which were swollen and more numerous than normal. The left kidney revealed vascular congestion and evidence of interstitial fibrosis in the superficial cortex. The left adrenal gland was normal. The right was markedly flattened and there was disruption of the normal levels by diffuse fibrosis. No nodules were present. The large tumor consisted of a thick fibrous wall containing cords of pale staining regularly arranged cells mostly resembling adrenal cortical cells. These cells were identified in most of the sections of the wall of the tumor. Prominent vascular thin wall spaces lay in the vicinity of these cells. The next interlayer consisted of a thick layer of fibrin and/or blood clot. The innermost layer consisted of necrotic tissue containing many neutrophils in cellular debris. Within this layer were foci of bacteria and fungi which on special staining were gram positive cocci and fungi resembling *Candida albicans.* It was concluded that a huge hemorrhagic cyst of the right adrenal gland occupied most of the right upper quadrant of the abdomen.

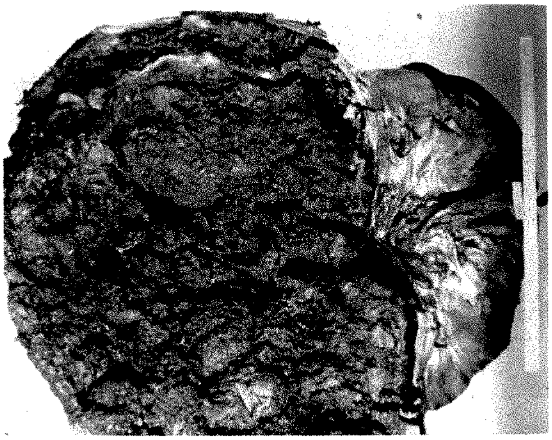


Fig. 3. K.C. The large tumor of the right adrenal gland attached to the right kidney, which was found at autopsy.

A liver scan of another patient (E.A.) and its diagrammatic interpretation are shown in Figure 4, *A* and *B*. At operation, a large retroperitoneal liposarcoma, 15 cm. in diameter, was found above the right kidney displacing the liver medially. An intravenous pyelogram disclosed that the right renal pelvis was displaced downwards and a cholecystogram demonstrated that the gallbladder was displaced to the left.

A comparison of the tumor size, the direction of growth and of the scans of the case reported and this one revealed a number of similarities, although in the latter case the tumor was less bulky and grew more in a downward direction. Displacement and protrusion into the liver were therefore less marked and this fact was evident in the scans; however, the semicircular scan defect in a position corresponding to the right lobe of the liver was strikingly similar. The scans show a gradual transition from an area of no activity at the edge of the liver to an area of lessened activity close to the midline and eventually this merges with an area of normal liver activity. The gradual transition in the activity could be explained on the basis of an expanding lesion causing a segment of the overlying liver to be wedge-shaped due to compression by an expanding tumor.

SCANNING TECHNIQUE

The standard magnascanner which has provision for dot recording and photorecording is employed. Radiopaque markers are placed on the patient and the scan is also marked at the same points. The scan can thus be superimposed on a roentgenogram. The latter is taken at a minimum focal skin distance of 72 inches to diminish magnification. The composite picture which is obtained from this procedure shows the position of the liver relative to the bony structures and the diaphragm. Major liver displacement, if present, will be evident. The edge of the liver or other palpable masses should also be outlined on the scan. We feel that Au^{198} gives a more reliable liver scan than rose bengal I^{131}. The liver margins are better outlined as there is no excretion of the isotope material into the gastrointestinal system or into the gallbladder.[1] Unless there is evidence of gross liver disease or some other contraindication, Au^{198} is used for all liver scanning. We have found that Au^{198} is concentrated in the spleen as well as in the liver, particularly if the liver is damaged from any cause.[1,2] From 100 to 300 μc of Au^{198} is used depending upon the weight of the patient and the probable size of the liver. Scanning is commenced ½ hour to 1 hour after the radioactive compound has been administered intravenously. A preliminary count rate survey of the chest and abdomen is made, using the 19-hole collimator at the detector-patient distance which gives the maximum count rate. The combination of scanning speed and dot factor (ratio of printed dots to radioactive events) is chosen so that two dots per millimeter will represent the maximum count rate. The adjustment for the photorecording part of the machine is based on a method of spreading the range of count rates from a maximum which corresponds to film density of 1.8 to a minimum which corresponds to 0.3 film density. With Au^{198} there is very little radioactivity outside the liver. The minimum count rate is usually due to radiation scattered from the liver or to penetration of the detector shielding. Nevertheless, we make no attempt to exclude this "patient background," as the margins of the liver can be easily delineated without employing

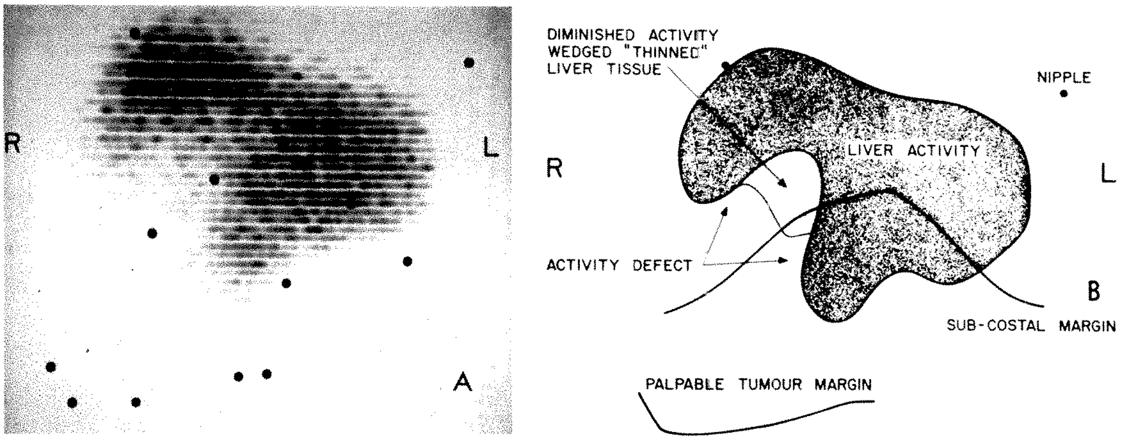


FIG. 4. E.A. (*A*) Au^{198} anterior liver scan with the nipples, sub-costal margin, edge of the tumor and the umbilicus indicated by the very black circular photodot marks. (*B*) Diagrammatic interpretation of *A*.

background erase. In many cases the spleen will be faintly outlined. If a high background erase were used, the faint splenic scintiscan would be excluded and diagnostic information lost.

SUMMARY

The liver scans of 2 patients with proven extrahepatic tumors exhibited defects in the radioactivity distribution which could have been incorrectly ascribed to masses in the liver. Both tumors originated from the right kidney region and expanded forward, displacing and indenting the liver, thus producing the liver scan defect.

The margins of the defects showed a transition from an absolutely "cold" area to an area of full radioactivity. This finding was presumably caused by thinning or wedging of a segment of liver by tumor compression.

Superimposition of the scan on a roentgenogram of the same region was undertaken in one case and the relationship of the liver to known landmarks made the direction and degree of liver displacement more apparent. Displacement of the liver was present in both cases.

Department of Radiology
Presbyterian-University Hospital
Pittsburgh 13, Pennsylvania

The author wishes to thank Mr. Richard C. Granke, S.B., for devising the method for setting the magnascanner controls, used for the scans. The technical assistance of Miss Charlotte Parrish, R.N., and Mr. Ronald Fabian, Isotope Technician, is gratefully acknowledged. The author also wishes to thank the Medical Illustrations Department for the reproduction of the scans and diagrams.

REFERENCES

1. Crespo, G. G., MacIntyre, W. J., and Christie, J. H. Comparison of I^{131} rose bengal and colloidal Au^{198} in liver scanning. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *88*, 296–303.
2. Gershon-Cohen, J., McClendon, J. F., and Sklaroff, D. M. Contrast roentgenography versus radioisotope scanning of liver and spleen. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1962, *88*, 304–310.

EXPERIMENTAL APPROACH IN THE USE AND MAGNETIC CONTROL OF METALLIC IRON PARTICLES IN THE LYMPHATIC AND VASCULAR SYSTEM OF DOGS AS A CONTRAST AND ISOTOPIC AGENT*

By PHILLIP H. MEYERS, M.D.,† FRANCIS CRONIC, M.D.,‡ *and*
CHARLES M. NICE, JR., M.D., PH.D.§
NEW ORLEANS, LOUISIANA

THE application of the basic principles of magnetism to biologic systems using small iron particles (1 to 3 μ in diameter) and/or metallic iron crystals (50–200 Ångstrom units in size) has been suggested.[1,2,4,5,6] We have conducted experiments to show that metallic iron particles can be used as contrast agents and magnetically controlled in the veins, arteries, lymph channels, and in the gastrointestinal tract. Experiments also show that radioactive metallic iron particles can be controlled and kept in a specific location *in vivo* and *in vitro* under certain conditions.

I. ROENTGENOGRAPHIC CONTRAST STUDIES

A. MAGNETICALLY CONTROLLED RADIOPAQUE IRON PARTICLES AS A CONTRAST AGENT IN THE VASCULAR, LYMPHATIC AND GASTROINTESTINAL SYSTEMS OF DOGS

Sixteen grams of iron particles (1 to 3 μ in size) were suspended in a mixture of 5 per cent dextran and saline (125 ml.) under constant agitation. Eight to 16 gm. of iron can also be suspended in 125 ml. solution of defibrinated dog's blood. Permanent magnets (external to the body of the dog) of approximately 5,000 gausses were held adjacent to the vessels and the gastrointestinal tract. Ten to 50 ml. of the above mixture was injected into the vessels or introduced into the gastrointestinal tract.

Figure 1 shows magnetic control of radiopaque iron particles held *in situ* in the vein by external magnets after intravenous injection. The roentgenograms were taken with conventional roentgenographic apparatus. After removal of the magnets and massage of the tissue, the iron particles were no longer visualized. Figure 2 is a femoral arteriogram of a dog. The external magnets hold the radiopaque iron contrast medium *in situ*. Figure 3 demonstrates the radiopaque contrast medium in the common carotid artery held *in situ* by external magnets after injection into the aortic arch via femoral catheterization. A lymphogram (Fig. 4) shows the radiopaque iron held *in situ* by external magnets. In Figure 5 external magnetic flux holds the iron particle contrast medium in the lower esophagus resulting in a controlled esophagram. In Figure 6 the iron particles are seen in the stomach with an external magnet held in close proximity, causing the iron particles to line up according to the lines of the magnetic field. This results in a controlled upper gastrointestinal series.

B. SUBCUTANEOUS INJECTION IN MICE, RATS, AND DOGS

A mixture of 8 gm. of micronized iron suspended in 10 ml. of peanut oil was prepared for subcutaneous injection. An injection of 0.5 ml. of this suspension was made into the base of the tail in 2 mice. Two control mice were injected similarly with 0.5 ml. of thorotrast. A small magnet was

---

* This work was supported by the following research grants: IN24D, American Cancer Society; #C-4581 (C2), James Picker Foundation, on recommendation of the Committee on Radiology, National Academy of Sciences—National Research Council, U.S.P.H.S.

† Assistant Professor, Department of Radiology, Tulane University School of Medicine.
‡ U.S.P.H.S. Fellow Trainee, Department of Radiology, Tulane University School of Medicine.
§ Professor and Chairman, Department of Radiology, Tulane University School of Medicine and Director of Diagnostic Radiology, Charity Hospital, New Orleans, Louisiana.

also attached with adhesive tape to the base of the tail overlying the area of the iron-peanut oil injection in one of the mice. The mice were placed in a plastic box which was radiolucent to the roentgen beam and roentgenography was easily performed. Roentgenograms were taken every 10 minutes for 30 minutes. Other roentgenograms were taken 45 minutes and approximately 4 hours later. For a period of 1 week additional roentgenograms were made 3 times a day, then once a week for 3 more weeks.

Two rats were given the same injection of 0.5 ml. of the micronized iron-peanut oil mixture and 2 rats were given thorotrast. The same sequence of roentgenograms was used.

Two dogs were anesthetized with intravenous sodium pentothal and 1 ml. of the iron-peanut oil mixture was injected into the tissues of one paw of each dog. An injection of 1.0 ml. of thorotrast was made into the paw of a control dog. No magnet was used. Roentgenograms were made using the same time sequence as in the mice and rats.

The results of injection of the micronized iron-peanut oil mixture and thorotrast into the tissues of the mice, rats, and dogs were as follows: with thorotrast the lymph nodes were visualized within 30 minutes following the injection. In the mice, rats and dogs, in which the iron-peanut oil mixture was injected subcutaneously with or without the magnetic attachment, there was no appreciable movement of the micronized iron-peanut oil mixture into the lymphatic systems in 4 weeks. It should be emphasized here that these injections were made directly into the tissue and not into the lymph channels or vascular system.

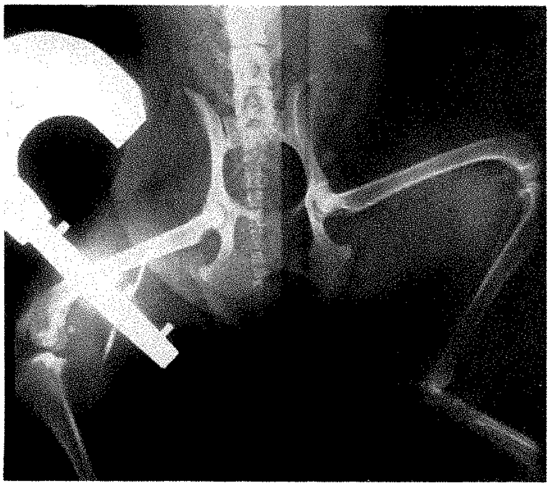


FIG. 1. Magnetic control of radiopaque iron particles held *in situ* in the vein by the external magnets after intravenous injection.

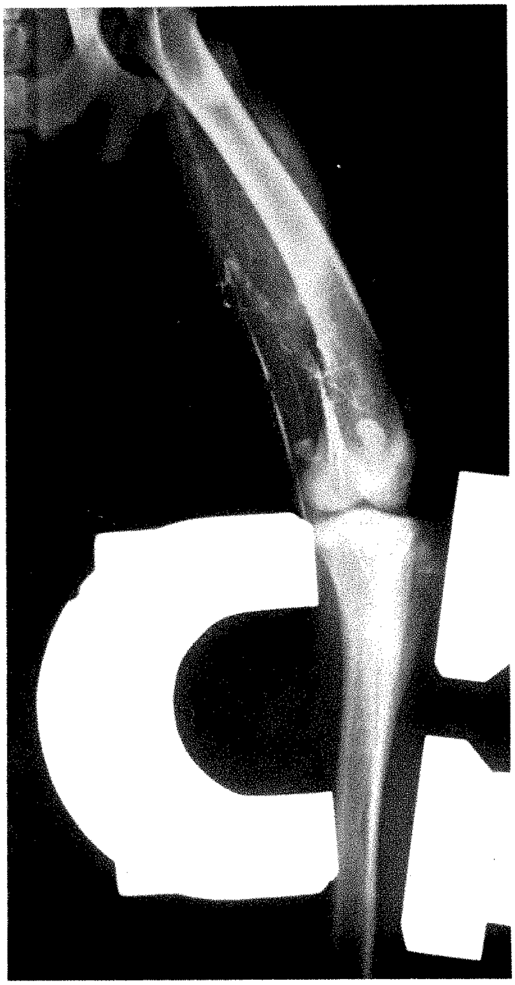


FIG. 2. Femoral arteriogram of a dog in which magnetic control of radiopaque iron particles was used.

II. RADIOACTIVE STUDIES

A. RADIOACTIVE IRON PARTICLES INJECTED INTO TISSUES OF MICE

Metallic radioactive iron particles in the 1 to 3 μ range were used for the radioactive

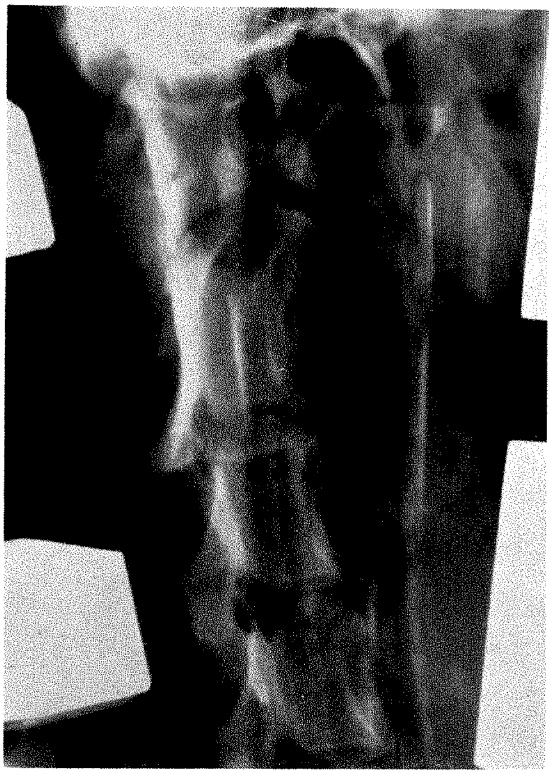


FIG. 3. Radiopaque metallic iron contrast medium in the common carotid artery held *in situ* by external magnets after injection into the aortic arch *via* femoral catheterization.

studies. These particles were sent to the Brookhaven National Laboratories where they were made radioactive. It was the purpose of this part of the experiment to determine the fate of radioactive Fe^{59} (half life 46.3 days) metallic particles injected directly into tissues of mice and to compare the fate of the Fe^{59} particles when injected directly into normal and roentgen irradiated mouse tissue. Forty-two mice were irradiated and separated into 7 equal groups; they were irradiated over a 10 day period in equal increments using 200 kv., 0.5 mm. Cu half value layer. The right leg and thigh were the areas of irradiation. Groups A, B, C, D, E, F, and G received 5,000, 4,000, 3,500, 3,000, 2,500, 2,000, and 1,500 r air dose, respectively. Three mice in each of the irradiated groups were not used further in the experiment and the radiation reactions were observed and compared with those of the remaining mice in each group. In those groups receiving above 3,500 r within 10 days, 1 to 2 mice died within 2 weeks. This was also observed in the control group. An amount of 0.5 ml. of radioactive metallic iron particles containing approximately 12 μc of Fe^{59} was injected into the irradiated tissue 2 weeks after the completion of irradiation. One mouse in each group was injected with 0.5 ml. of thorotrast into the irradiated region 2 weeks after the completion of the irradiation. A dual scintillation detection system consisting of 2 sodium iodide crystals, 2 rate meters, and 2 recorders operating simultaneously, was

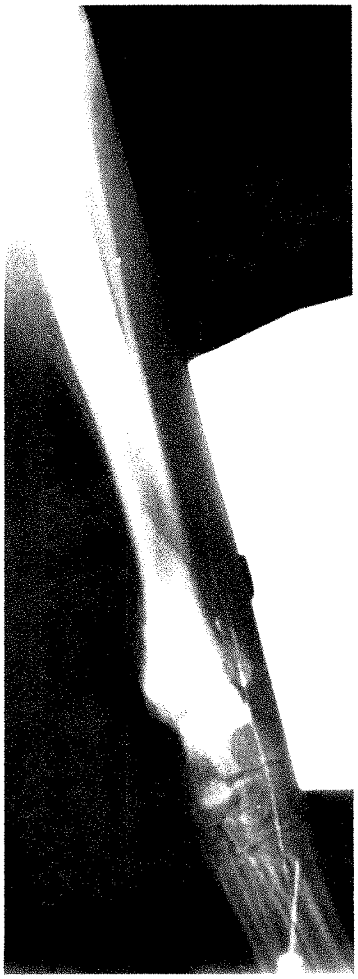


FIG. 4. Lymphogram shows the radiopaque iron held *in situ* by external magnets.

used in these experiments. The mice that were injected with radioactive Fe^{59} had daily tracings for 3 weeks with one iodide crystal placed over the region of the injection site, *i.e.*, over the site of the irradiated tissue, and the other iodide crystal placed over varying parts of the body. The irradiated mice injected with thorotrast were followed daily for 3 weeks with roentgenograms.

Ten unirradiated mice were injected with 12 μc of radioactive iron suspended in 0.5 ml. absolute alcohol into the same region as those mice which were irradiated. These unirradiated mice were also followed with the dual scintillation system daily for 3 weeks.

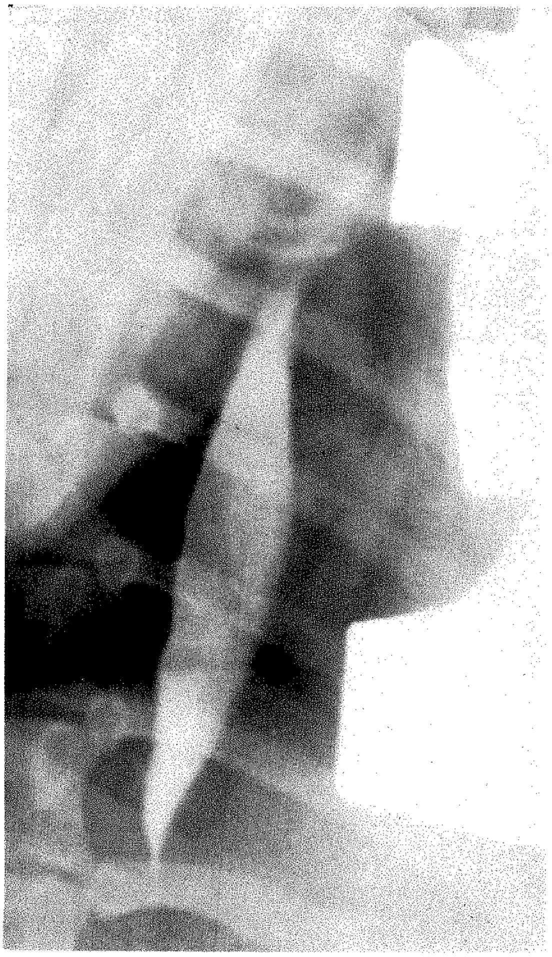


Fig. 5. An external magnetic flux holds the iron particle contrast medium in the lower esophagus, resulting in a controlled esophagram.

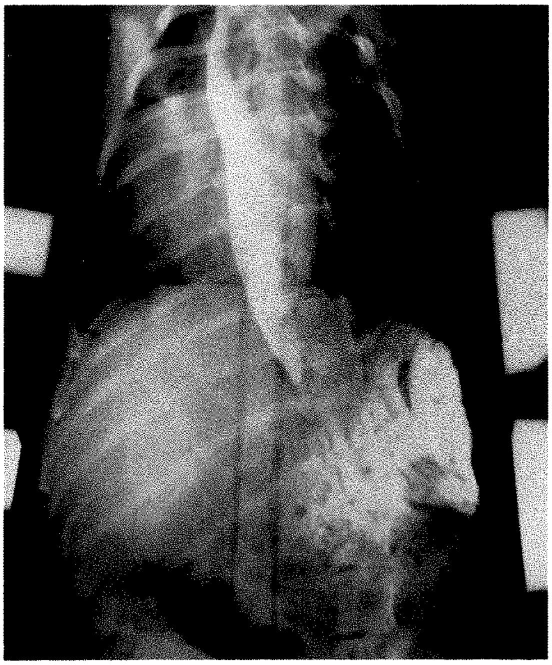


Fig. 6. The iron particles are seen in the stomach with an external magnet held in close proximity, causing the iron particles to line up according to the lines of the magnetic field.

The results demonstrated that there was no appreciable difference in the fate or movement of the radioactive iron particles over a 3 week period following injection into irradiated and nonirradiated tissue. In both groups the radioactive iron remained *in situ* and did not move out of the tissue area to any appreciable extent. The mice which had the thorotrast injection showed no movement of the thorotrast from the injection site. This may indicate blockage of lymphatics secondary to irradiation since in nonirradiated mice thorotrast moved into the lymphatics within 30 minutes after injection.

B. MAGNETICALLY CONTROLLED RADIOACTIVE IRON PARTICLES INJECTED INTO THE VASCULAR SYSTEM OF DOGS

In vivo studies consisted of the injection of radioactive metallic iron particles into the vascular system of dogs. Permanent magnets of approximately 5,000 gausses were placed so as to surround the lower tibia. A dual scintillation detector system over the magnetic area and outside of the magnetic field, recording simultaneously, showed that the radioactive iron particles could be held in a specific location *in vivo.*

The first experiment was an injection of $\frac{1}{8}$ mc of radioactive Fe^{59} into the right femoral artery, 9 inches proximal to a round doughnut shaped magnet of approximately 5,000 gausses into which the dog's leg was placed. Dual simultaneous recordings were made of this experiment. The readings showed a marked rise in radioactivity (over the region of the round magnet); *i.e.*, the magnet has held the radioactive Fe^{59} *in situ*, indicating that it is possible to magnetically control radioactive iron particles in the vascular system. The tracings showed radioactivity which was equal to the background over the animal tissue at a site distal to the region of the magnet. This demonstrated that the magnet held practically all of the radioactive iron particles that were injected intra-arterially, proximal to the magnetic field.

Simultaneous dual recordings were made after the injection of $\frac{1}{8}$ mc of Fe^{59} metallic particles into the right lower femoral artery. The tracings over the noninjected lower left leg, after injection of the right femoral artery with Fe^{59}, showed that there was no appreciable increase in radioactivity as compared to background recording. The tracings made over the upper left extremity showed the same results.

The tracings over the liver demonstrated that there was a slight deposition of Fe^{59} in this organ. The readings also revealed a slight deposition of Fe^{59} in the spleen, a smaller amount than in the liver. The tracings retaken over the site of injection showed (also seen visually) that there was some leakage of radioactive material, *i.e.*, leakage of blood about the needle puncture site, with a resultant high reading. The tracings corresponding to the area of the round magnet (over the right thigh) demonstrated that there was magnetic control of the radioactive iron metallic particles in the vascular system. Background tracings recorded at the same time as the readings over the lower right paw of the dog gave identical results, indicating that no appreciable radioactive material had flowed distal to the right thigh region where the magnet was "holding" the Fe^{59} metallic particles.

Two days after the injection of $\frac{1}{8}$ mc of Fe^{59} into the femoral artery (the magnet was removed within 1 hour after the injection), the tracings demonstrated residual radioactivity in the tissue area over the site of the injection due to leakage of the radioactive material during the time of injection. Another high peak of residual radioactivity, revealed by the dual scintillation system and recorder, was at the site of the magnet over the right thigh. This most likely represented iron particles 1 to 3 μ in diameter that had been pulled through the artery into the tissues by the magnetic field 2 days earlier. Multiple simultaneous readings over the other extremities demonstrated slight radioactivity in the body tissues; however, in general, the tracings showed substantially less radioactivity here than over the injection site and the site of the magnet. The readings taken over the liver and spleen showed a slight minimal increase in radioactivity as compared to the extremities. This most likely represented deposition of iron particles in the reticuloendothelial system.

Four days after the intra-arterial injection of radioactive Fe^{59}, the tracings showed some remaining radioactivity over the site of injection. There was a substantial decrease in the radioactivity over the site of the magnet as compared to that of previous days and the radioactivity over the other extremities likewise showed a continued decrease. The liver and spleen exhibited a slight increase in radioactivity which probably meant that a slight increase in deposition of radioactive material in the reticuloendothelial system occurred.

Tracings taken 7 days after intra-arterial injection of Fe^{59} revealed a marked decrease in radioactivity over the site of the round magnet as compared to that of previous days while the liver and spleen showed a continuing slight increase. The extremities showed a general decrease in radioactivity.

Two weeks after the injection of Fe^{59} intra-arterially, the tracings disclosed remaining radioactivity over the site of injection. There was a continuing decrease in radioactivity over the site of the magnet when compared to that of previous days, and the liver and spleen similarly showed a decrease in radioactivity. The extremities showed minimal radioactivity.

Thus these studies proved that the magnetic field had the following major effects:

1. At the time of injection it held *in situ* essentially most of the radioactive material that was actually injected and which had not leaked out around the injection site.

2. The magnetic force of approximately 5,000 gausses pulled the Fe^{59} into the tissues surrounding the blood vessels or into the wall of the blood vessel itself at the magnetic site.

3. Some radioactive material remained at the site of injection, slowly decreasing over a 2 week period. Within a week the liver and spleen exhibited a gradual increase in radioactivity and then a decrease, indicating that the reticuloendothelial system continued to hold the radioactive material and that during the second week the material was depleted from the system.

C. RADIOACTIVE IRON PARTICLES INJECTED INTO THE VASCULAR SYSTEM OF DOGS WITHOUT BEING MAGNETICALLY CONTROLLED

One-eighth of a millicurie of radioactive iron particles was injected intravenously in the right femoral vein of another dog. A magnet was not used in this experiment. Tracings showed that there was a substantial increase in radioactivity in the liver. The spleen also showed an increase in radioactivity but not as much as the liver. Readings over the extremities revealed a general increase in radioactivity but not comparable to that of the liver and spleen. Readings taken 1 day after the intravenous injection of radioactive Fe^{59} disclosed essentially the same findings. Readings taken 2 days after the intravenous injection showed no appreciable change. Readings taken 15 days after the intravenous injection revealed minimal residual radioactivity over the liver and spleen. Multiple readings over both kidneys from anterior, posterior, and lateral directions indicated at 15 days the same radioactivity as in the extremities and head.

Separate intravenous and intra-arterial injections of radioactive iron particles in different dogs were made to evaluate the radioactivity in the kidney and brain in comparison to that of the other organs. These tracings demonstrated that there was no appreciable difference in the radioactivity of the kidney regions and brain as compared to that in the other body tissue except over the liver and spleen. The liver showed substantial increase in radioactivity after intravenous and intra-arterial injection.

Radioisotope scans of the dog's body including special attempts to scan the liver and kidneys and bladder failed to yield a hepatogram, renogram or cystogram.

III. PATHOLOGIC STUDIES

Gross anatomic studies of the brain, kidneys, liver, heart, lungs, and muscles in a dog that was sacrificed within 1 hour after the injection of 10 gm. of micronized iron 1 to 3 μ in size suspended in 100 ml. of dextran showed no thrombi in the major vessels nor any iron in the organs. No emboli were noted.

Gross examination of the organs 2 weeks after a lymphatic injection of 50–200 Ångstrom units of iron particles revealed no evidence of thrombosis or other pathologic lesions.

Microscopic studies were performed in a dog 1 hour after the injection of 1 to 3 μ iron particles. Approximately 10 gm. of micronized iron was suspended in 100 cc. of dextran; 50 cc. of this mixture was injected intravenously and the contrast medium was held in the femoral vein. Fifty milliliters of the dextran iron suspension were injected into the femoral artery of the same dog and held *in situ* by magnetic fields external to the dog and a femoral arteriogram was made. The dog was sacrificed 1 hour after the injection.

Hematoxylin and eosin and Gömöri's iron stains were used on tissues from all of the organs. These special iron stains demonstrated a great quantity of micronized iron in the liver lobules, portal veins and hepatic arteries. The spleen showed thrombi of the veins. The iron particles were seen in abundance in the splenic arteries and in the red pulp. In the kidneys the iron was almost totally selectively concentrated in the glomeruli (Fig. 7). No iron particles were noted in the brain, either by the special iron stain or the hematoxylin and eosin stains. The lungs showed very highly concentrated iron particles throughout the tissue. In the muscles, numerous particles were seen between the vessels and the muscle bundles. The heart showed only some iron. It should be emphasized that these findings were within 1 hour after injection of the micronized iron contrast medium.

In another dog, 10 gm. of iron particles, which were 50–200 Ångstrom units in size, were mixed with 50 ml. of blood, 50 ml. of 5 per cent dextran and 2 cc. of heparin and injected intra-arterially. No magnetic field was used. The dog was sacrificed 2 weeks later. Special Gömöri iron stains were made on all of the organs. The liver showed frequent but sparse amounts of iron particles, in the reticuloendothelial cells. The spleen showed infrequent iron particles in the histiocytes, phagocytes, and red pulp

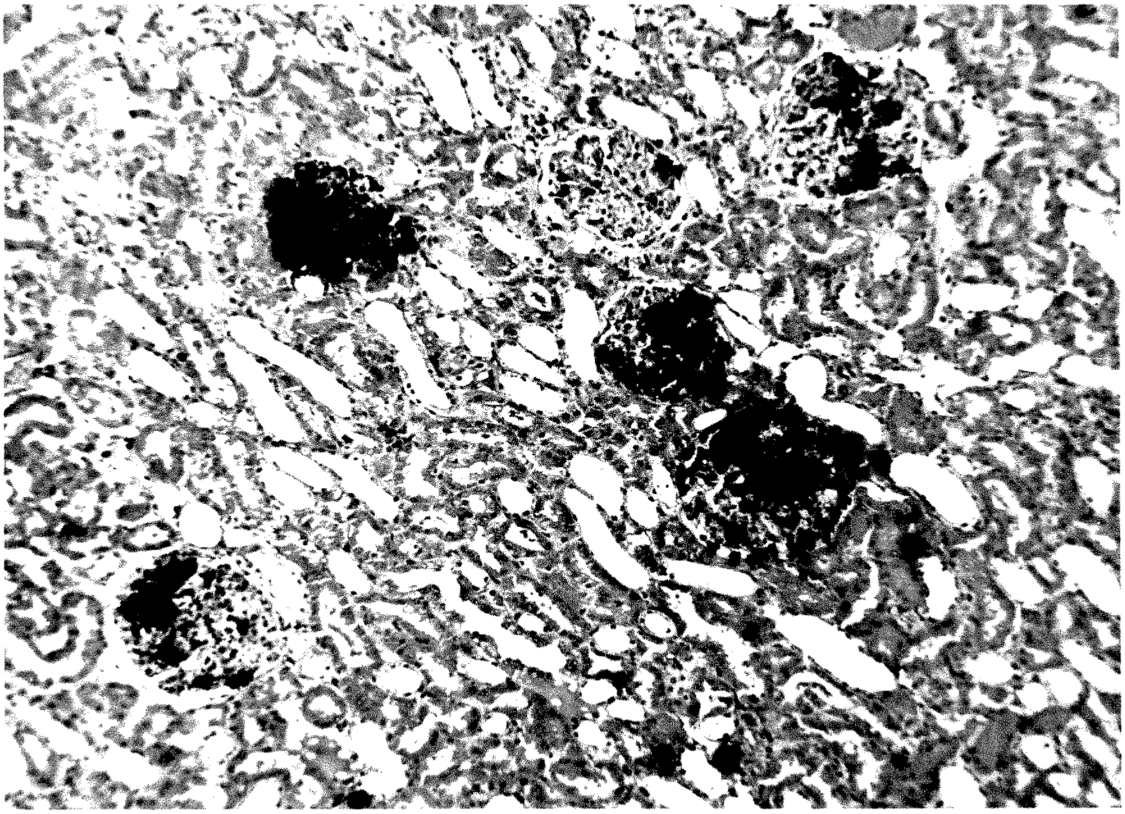


Fig. 7. In the kidneys the iron was almost totally selectively concentrated in the glomeruli within 1 hour after intra-arterial injection of iron particles (×76).

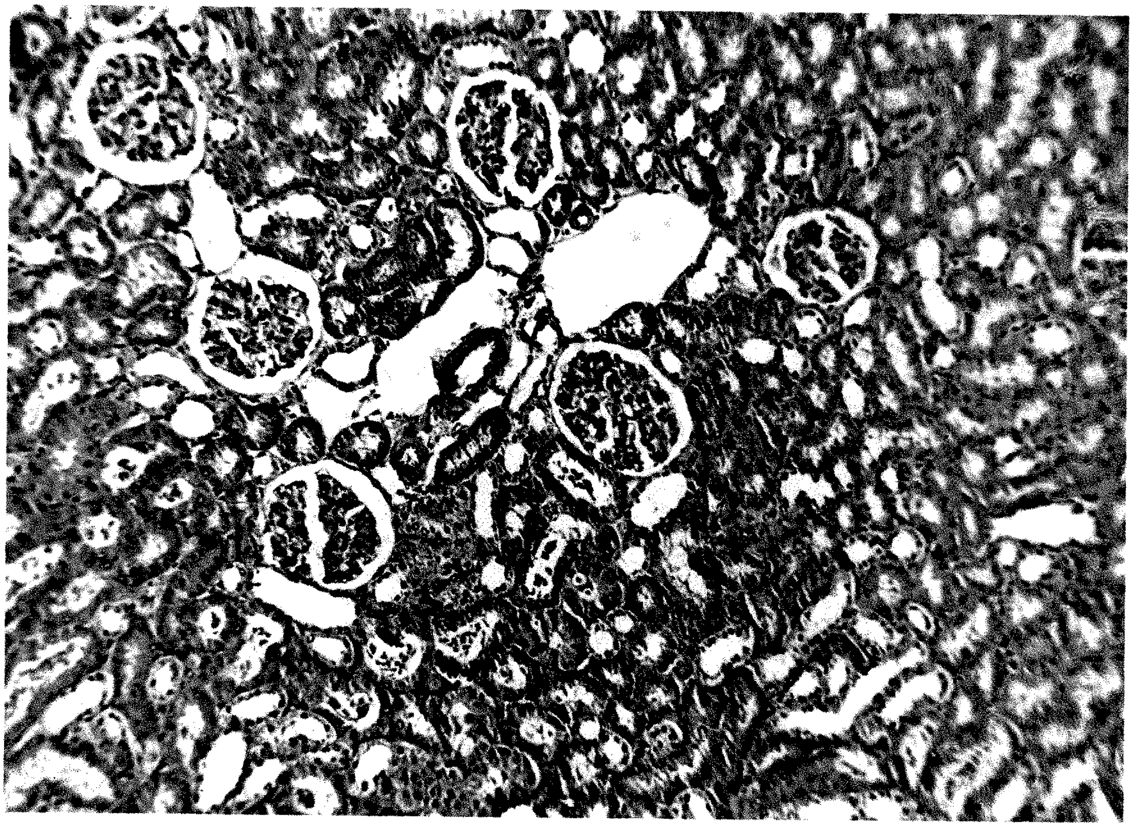


Fig. 8. Sections of kidneys 2 weeks after intra-arterial injection of radiopaque iron particles show no evidence of iron particles (×76).

There were some iron particles in the walls of the small veins. Neither the sections of the kidneys (Fig. 8) nor of the brain showed any evidence of any iron particles. In the lung, some particles were noted but were rare. No iron particles were visualized in the sections of muscle, pancreas, and heart tissue.

The dorsal lymph channel of a paw in a third dog was catheterized and 10 gm. of micronized iron suspended in 100 ml. of 5 per cent dextran was injected and held *in situ* by external magnets. This dog was sacrificed 2 weeks after this injection. Hematoxylin and eosin and Gömöri iron stains were made on all of the organs. The hematoxylin and eosin stain did not demonstrate the iron very well. The stains showed no iron in the sections of brain, muscle, pancreas, heart, and kidney (Fig. 9). In the spleen iron particles in phagocytes, histiocytes, and red pulp were found but rarely. The lungs showed small amounts of iron in the alveolar walls when the special iron stain was used, but infrequently.

DISCUSSION

The injection of iron particles suspended in a chelating agent such as desferrioxamine B[3] should be helpful in eliminating the iron particles from the body of the experimental animal. Desferrioxamine B has been used for the removal of iron particles within the reticuloendothelial system in patients with siderosis and hemachromatosis. It is emphasized, however, that this procedure is experimental and the toxicology of the iron particles has not been investigated fully. We do foresee the possibility that a magnetic flux could be concentrated

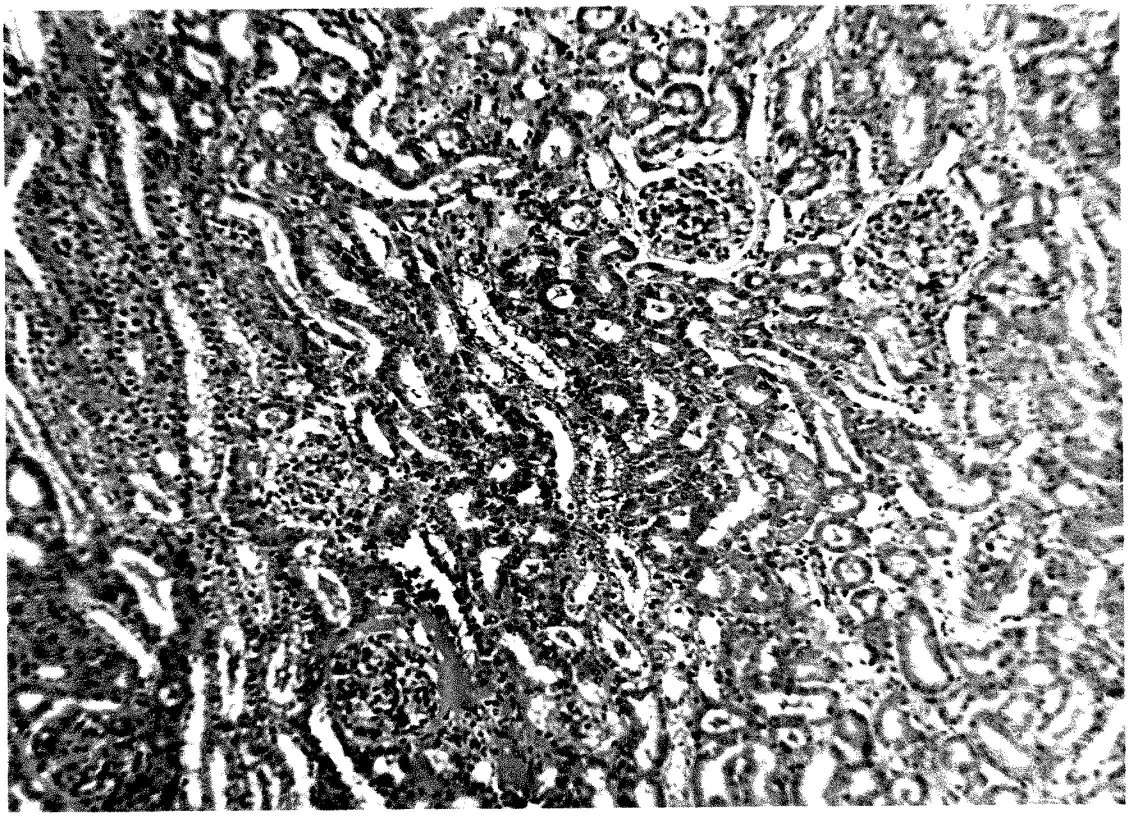


Fig. 9. Two weeks after a lymphogram no iron particles are seen in the kidney (×76).

on certain tissue by injection of the iron particle suspension. After injection, the iron particles could be held *in situ* by the magnetic field and then the necessary roentgenograms of the vessels and/or gastrointestinal tract could be made without the use of automatic serial roentgenographic devices.

It is interesting that the microscopic and gross studies showed that after 2 weeks there were were exceedingly small amounts of iron in the body tissues. This correlated well with the radioactive studies.

The development of advanced technology in the use and control of metallic iron particles *in vivo* may result in the following:

1. A new technique in radiation therapy, *i.e.*, placement in specific tissue areas of radioactive metallic particles by magnetic field forces.
2. Development of magnetically controlled radiopaque contrast medium.
3. A technique using iron particles as vehicles for carrying chemotherapeutic agents and for carrying radiation of selected energies by coating the iron with other metals.
4. A technique of incubation of these particles or of combinations of these metallic particles with conventional organic iodide radiopaque contrast media under magnetic control.
5. A technique of mechanical activation of iron particles which have previously been localized in specific tissue by ultra high frequency devices or by alteration of magnetic fields.

SUMMARY

An experimental approach in developing magnetically controlled radiopaque iron metallic particles as a radioisotopic radiocontrast agent in dogs in the vascular and

lymphatic systems is described.

It has also been shown that one can magnetically control radioactive iron particles in the vascular system. Injection of radioactive and nonradioactive iron particles directly into healthy animal tissue or irradiated animal tissue results in these iron particles remaining in the tissue with no appreciable movement. Gross, histologic and radioisotopic studies show interesting possibilities as to the future use of these particles.

Phillip H. Meyers, M.D.
Department of Radiology
Tulane University School of Medicine
New Orleans 12, Louisiana

REFERENCES

1. Barnothy, J. M., Barnothy, M. F., and Boszormenyi-Nagy, I. Influence of magnetic field upon leucocytes of mouse. *Nature,* 1956, *177,* 577–578.
2. Barnothy, M. F., and Barnothy, J. M. Biological effect of magnetic field and radiation syndrome. *Nature,* 1958, *181,* 1785–1786.
3. Ciba Pharmaceutical.
4. Freeman, M. W., Arrott, A., and Watson, J. H. L. Magnetism in medicine. *J. Appl. Physiol.,* Suppl., 1960, *31,* 404–405.
5. Levine, S. Magnetic techniques for in vitro isolation of leucocytes. *Science,* 1956, *123,* 185–186.
6. Meyers, P. H., and Nice, C. M., Jr. Future trends in radiological research. *Bull. Tulane Med. Fac.,* 1962, *21,* 75–79.

◆

"SECOND-LOOK" LYMPHOGRAPHY*

By RUHERI PEREZ-TAMAYO, M.D., JOHN R. THORNBURY, M.D., *and*
R. JAMES ATKINSON, Capt. USAF (MC)†
DENVER, COLORADO

"SECOND-LOOK" lymphography is the re-examination of the lymphatic system by lymphography with the advantage of a baseline study done previously for comparison. We have utilized this technique at the University of Colorado Medical Center to investigate changes in the lymphatic system configuration as a result of: (1) surgical treatment or radiation therapy and (2) progression of the disease process.

LIMITATIONS OF LYMPHOGRAPHY

The limitations of lymphography are those inherent in the currently used method as well as those due to disease itself. These are:

1. The range of normal variation in lymph node pattern is great, and benign processes (fat replacement, fibrosis, inflammation)[3] will produce changes that simulate lymph node metastases. In addition, minute metastases which can be seen on microscopic sections of lymph nodes cannot be discerned on the lymphogram.
2. Adequate, consistent filling of some of the lymph node groups, important in routes of lymphatic metastatic spread, is not obtained. When lower extremity injection is utilized, these include obturator, hypogastric, and mesenteric lymph nodes.[4]
3. When a lymph node is completely replaced by tumor, contrast material cannot enter the lymph node architecture to demonstrate the filling defect required for diagnosis of metastasis.[8]
4. Excessive uptake of contrast material by tumor-distorted lymph nodes and trunks can prevent adequate contrast filling of more proximally involved lymph nodes.
5. A single examination shows only one phase of a changing, malignant process.

The use of lymphography in treatment planning should take into account these limitations. Lymphography should be used to complement clinical experience and knowledge of the natural history of progression of cancer. The "second-look" has not eliminated any of the limitations mentioned, but it does provide additional evidence of the course of disease. It has shown interesting findings in the lymphatic system of patients with malignant disease treated by radiation therapy or surgery. In some cases, lymphography has demonstrated the extent of disease beyond the capability of other diagnostic means.

METHOD

The method of lymphography used was a modification of that pioneered by Kinmonth *et al.*[5,6] in England and more recently described by Wallace *et al.*[9] This involves injection of contrast material (ethiodol*) via a lymph trunk cannulated in the dorsum of each foot. Roentgenograms are taken during the course of injection for demonstration of lymph flow and trunk configuration. Additional roentgenograms are obtained on the day after injection to show lymph node detail. The second lymphography was performed through cannulation of a lymph trunk lateral to that used in the first study. Our investigation has been restricted to pelvic and retroperitoneal tumors, utilizing bilateral lower extremity injection. Thus, the inguinal, iliac, and abdomino-aortic lymph nodes have been the groups under study.

"Second-look" lymphography has shown

---

* A portion of the ethiodol was made available by E. Fougera and Co., Inc., Hicksville, New York.

* Presented at the Forty-fifth Annual Meeting of the American Radium Society, San Francisco, California, April 1–4, 1963.

This study has been supported by a grant from the Milheim Cancer Foundation, Denver, Colorado.

† The contents of this article represent the personal views of the Air Force author and are not to be construed as a statement of official Air Force policy.

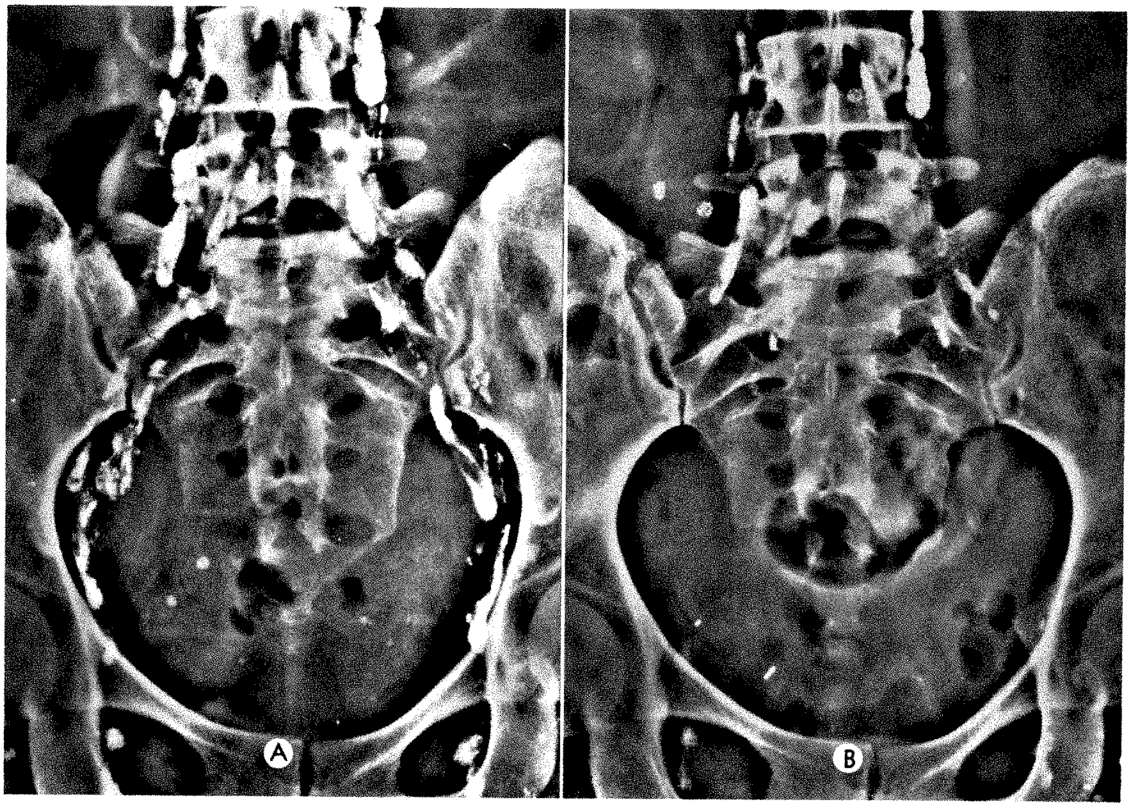


Fig. 1. Case 1. (*A*) Preoperative lymphogram showing normal lymph node configuration. (*B*) Postoperative roentgenogram showing surgical removal of all but several small presacral lymph nodes after pelvic lymphadenectomy.

that: (1) radical lymph node dissection in the pelvic or retroperitoneal region does not result in complete removal of all lymph nodes in the region; (2) severe lymphatic obstruction due to tumor can be relieved by radiation therapy in the case of radiosensitive tumor. Concomitant development or utilization of collateral lymph trunks has been observed; and (3) progression of disease, despite surgery or radiation therapy, has been manifested by further lymph node and trunk distortion with increasing severity of lymphatic obstruction. Utilization of lymphatico-venous anastomoses by contrast material following this route of potential path of metastasis has been demonstrated.

Three representative cases and selected roentgenograms are presented to illustrate these points.

REPORT OF CASES

Case 1 (CGH #178314). This 36 year old woman was treated at another hospital, 1 year prior to admission, with telecobalt and intracavitary radium for carcinoma of the cervix, staged League of Nations II. She was subsequently referred to Colorado General Hospital after biopsy evidence of recurrence was obtained by her gynecologist. For 2 months prior to admission, she had progressive lower abdominal and right thigh pain, vaginal discharge, and weight loss. An ulcerating lesion replacing the cervix, indurating the right parametrium, and extending close to the right pelvic wall was found on clinical examination. Routine roentgenograms and a lymphogram (Fig. 1*A*) showed no abnormality.

At operation, the tumor was found to extend to the right pelvic wall, but was not fixed to it. Radical hysterectomy with pelvic lymphadenectomy was performed, and the surgeon considered the tumor completely removed. Two lymph nodes in the right medial external iliac chain were completely replaced by tumor in the surgical specimen. No contrast material in these two lymph nodes was seen on the surgical specimen roentgenogram. A postoperative roentgenogram (Fig. 1*B*) showed all the contrast-filled lymph nodes with the exception of a few small presacral lymph nodes to have been removed.

She returned four months later with a painless, fixed, 3 by 4 cm. right inguinal mass. A "second-look" lymphogram (Fig. 2, *A* and *B*) showed bilateral changes secondary to lymphadenectomy plus partial lymphatic obstruction. There was a right inguinal lymph node filling defect that was not seen on the first lymphogram. Collateral channels to normal-appearing presacral lymph nodes were present. Also noted was a collection of contrast material in a space in the left external iliac region considered to represent a lymphocele secondary to the previous lymphadenectomy. Subsequent right inguinal lymph node dissection showed a tumor mass in the right perivesical area extending directly to the inguinal region. Two of 14 inguinal lymph nodes were positive: one lymph node produced a defect on the lymphogram, and the other contained contrast material but appeared normal on the lymphogram.

CASE II (CGH #161346). One year previously, this 36 year old woman had undergone radical hysterectomy and pelvic lymphadenectomy for endometrial sarcoma with invasion of the cervix. For 2 months prior to admission, she had increasing lumbosacral pain with radiation to the left thigh. Clinical examination revealed a 10 cm. in diameter fixed mass in the left posterior pelvis. An intravenous pyelogram showed left hydronephrosis.

A lymphogram (Fig. 3, *A* and *B*) showed changes secondary to lymphadenectomy, venous filling, lymphatic obstruction, and left external iliac lymph node metastases. Pelvic lymphatico-venous anastomoses were utilized with diffuse contrast material embolization to the lung. This was asymptomatic. The common iliac trunks were displaced laterally and anteriorly by a presacral mass that was not suspected clinically. The common iliac veins were almost completely obstructed by this mass on a cavagram.

At laparotomy, involvement of the two areas

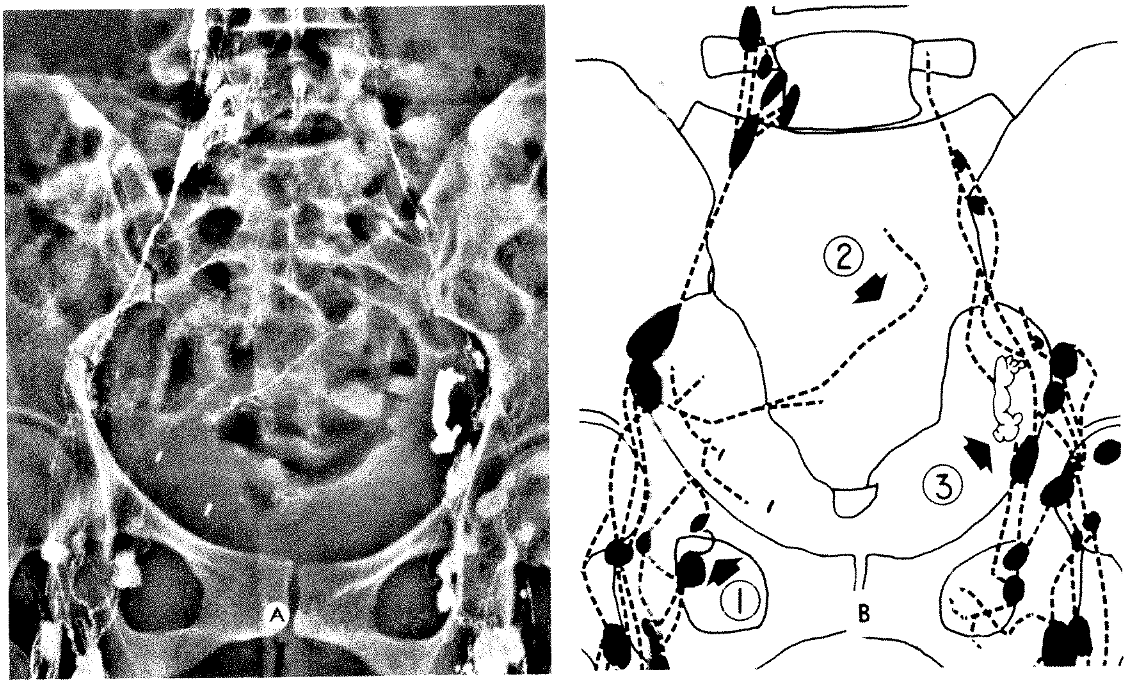


FIG. 2. Case I. (*A*) "Second-look" lymphogram (during injection) done 4 months after pelvic lymphadenectomy. (*B*) Diagram of *A* showing (1) rim of contrast material in invaded inguinal lymph node, (2) collateral trunk to presacral lymph node area, and (3) lymphocele. Sparse-appearing trunks and partial lymphatic obstruction are secondary to lymphadenectomy.

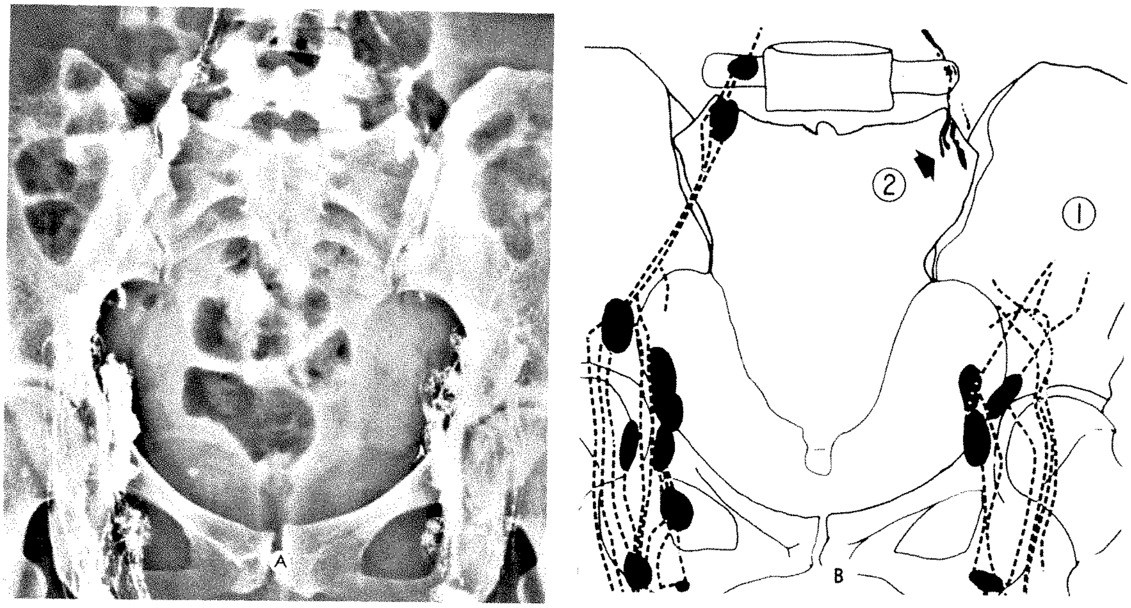


Fig. 3. Case II. (*A*) Lymphogram (during injection) from first study. (*B*) Diagram of *A* showing (1) lymphatic obstruction and (2) venous filling. Sparse iliac trunks and lymph node absence are due to previous pelvic lymphadenectomy.

was confirmed with the presacral mass fixed to bone. Clips were left for localization, and palliative radiation therapy was instituted. The pelvic masses initially regressed remarkably, but rapidly recurred. Mediastinal and pulmonary metastases developed, and transient palliation was achieved by radiation therapy.

A "second-look" lymphogram (Fig. 4, *A* and *B*) after the pelvic masses escaped control, showed increasing lymphatic obstruction and associated venous filling. There was utilization of pelvic lymphatico-venous anastomoses lead-

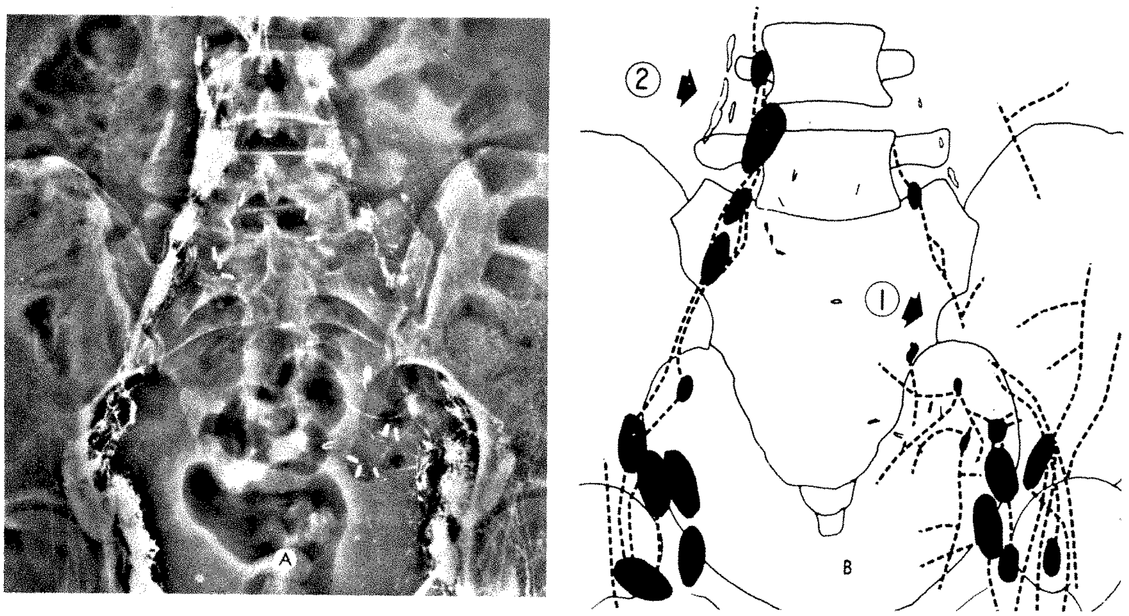


Fig. 4. Case II. (*A*) "Second-look" lymphogram (during injection) done 2 months after the first study. (*B*) Diagram of *A* showing (1) increasing lymphatic obstruction and (2) venous filling.

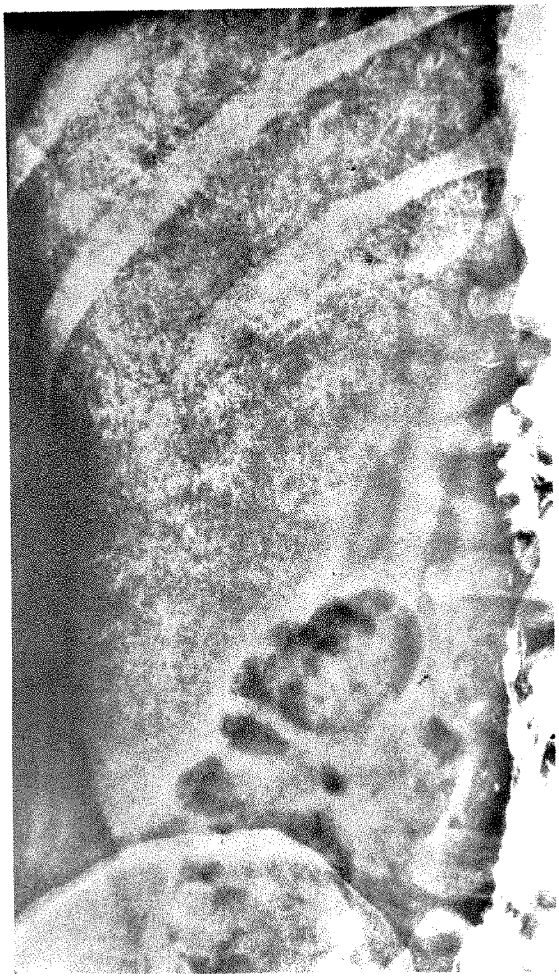


Fig. 5. Case II. "Second-look" lymphogram showing deposition of contrast material in the liver. This was due to concomitant severe vena cava and iliac lymphatic obstruction with utilization of lymphatico-venous anastamoses from iliac lymph nodes to the portal system.

ing to the portal system with contrast material deposited in the liver (Fig. 5) early in the course of injection. The patient expired at home 1 month later, but no autopsy was obtained.

Case III (CGH #175518). Upon admission, this 45 year old man was severely ill, presenting with right pulmonary infarction, a mass filling and distending the abdomen, extensive abdominal wall collateral circulation, and bilateral lower extremity edema. The right testis was not palpable in the scrotum or inguinal canal. Lymphograms (Fig. 6, *A* and *B*) showed severe lymphatic obstruction due to a huge mass distorting the trunks and lymph nodes in the iliac and abdomino-aortic regions. The extent of the mass was more accurately shown by the lymphogram than by clinical palpation. An inferior vena cavagram showed complete caval obstruction and renal displacement.

Laparotomy revealed a very friable mass filling most of the abdomen and extending into the pelvis. The liver was normal. Biopsy of the mass demonstrated metastatic seminoma, and this was the only tissue removed.

The entire pelvis and only the medial portion of the abdomen received a slow course of radiation therapy. The kidneys were spared. Serial roentgenograms (Fig. 7, *A* and *B*) showed rapid, remarkable regression of the mass as delineated by residual contrast material. The regression was by a "rolling in" of the lateral margins of the mass. No lesion was palpable 2 months after the start of therapy, and the collateral circulation and peripheral edema disappeared.

"Second-look" lymphograms (Fig. 8, *A* and *B*) done at the termination of therapy, showed extensive collateral trunks not present on the first examination. There was venous filling present, but there was no resultant roentgenographic evidence of oil embolization. Only a vestige of tumor remained. Inferior vena cavagrams (Fig. 9, *A* and *B*) now showed normal flow with mild defect and displacement by the residual mass. He has continued to do well and is without evidence of disease 10 months after the start of therapy.

DISCUSSION

Case I well demonstrates the false sense of security fostered by an apparent clean sweep of the pelvic lymph nodes suggested by the postoperative roentgenogram. The actual situation was indicated by the fact that the involved lymph nodes in the surgical specimen were *completely* replaced by metastases. This emphasizes the fact that completely replaced lymph nodes cannot be shown objectively on lymphography, as also noted by other investigators.[8]

This case also illustrated the point that multiple small lymph nodes remain after the most meticulous lymphadenectomy, and collateral channels serve them after radical operation. It is surprising how

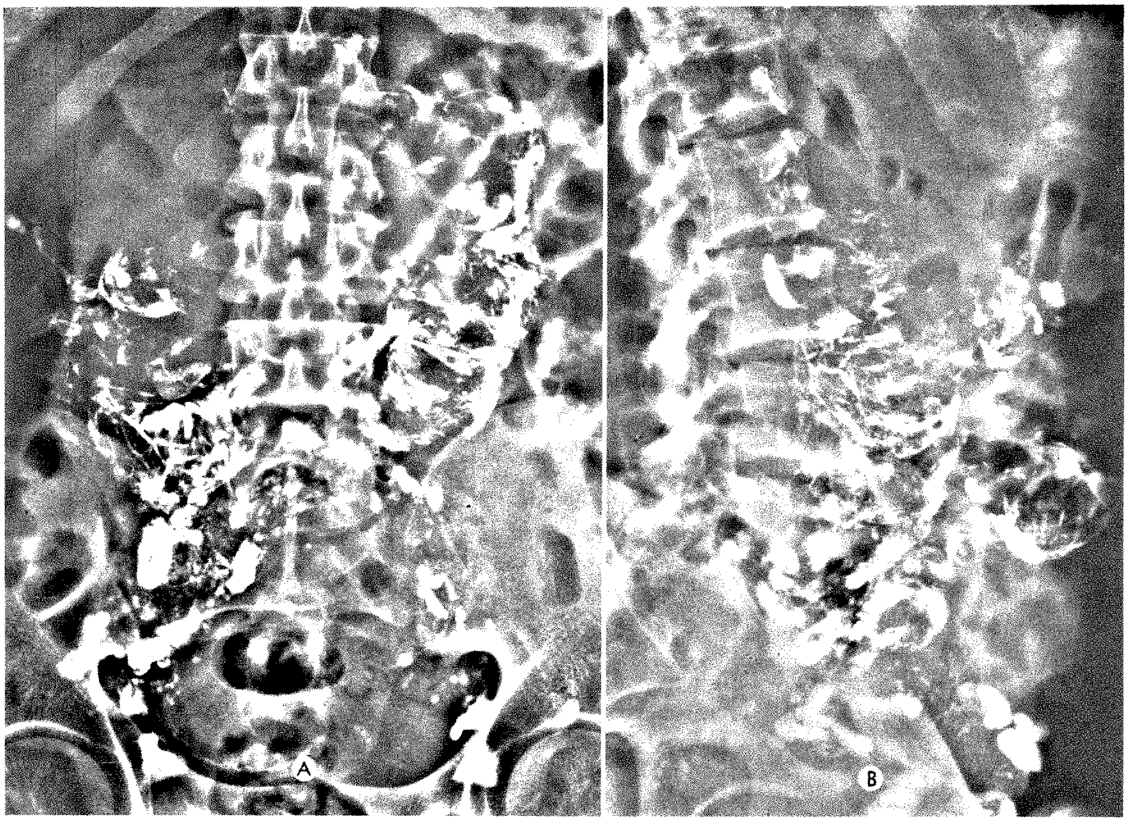


FIG. 6. Case III. (*A* and *B*) Anteroposterior and lateral roentgenograms from the first study showing a large mass due to metastatic seminoma distorting the iliac and abdomino-aortic lymph nodes and trunks.

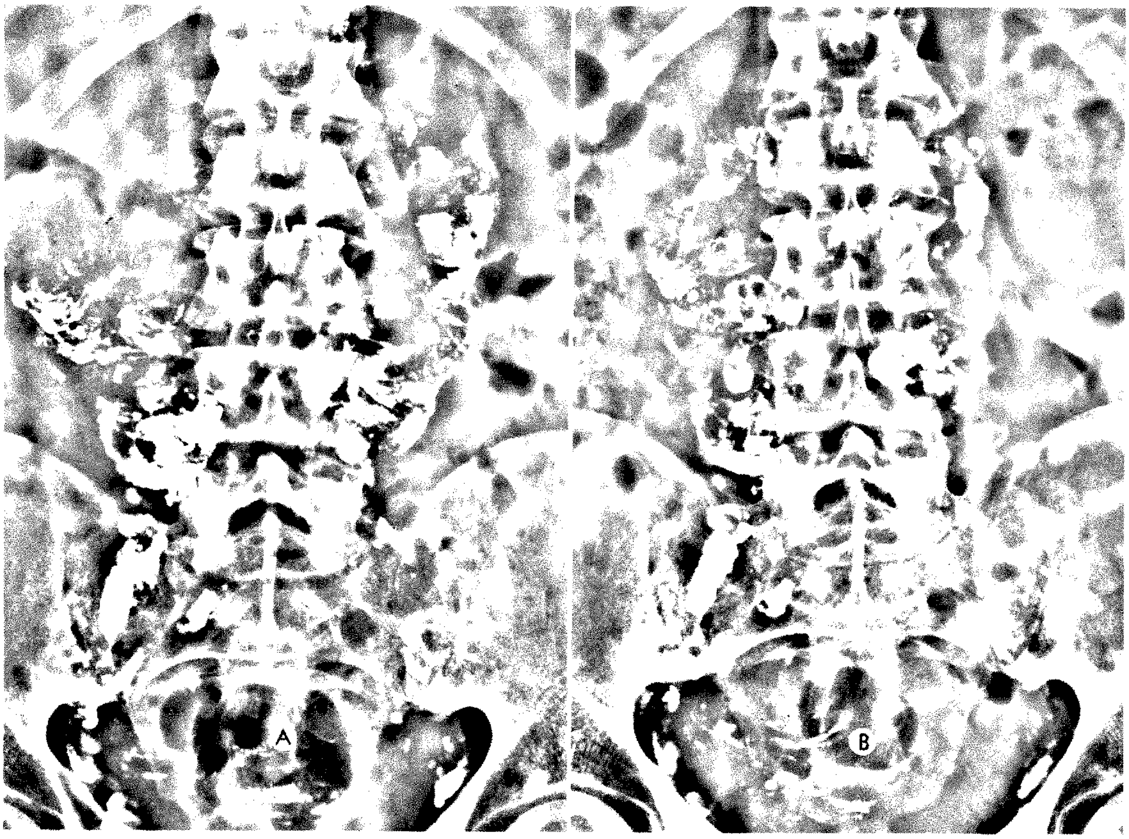


FIG. 7. Case III. (*A*) August 10, 1962. (*B*) September 6, 1962. Roentgenograms taken during the course of radiation therapy demonstrating regression of the tumor mass.

severe the compromise of lymphatic flow can appear on the lymphogram, and peripheral edema not ensue. At present, 2 months postoperatively, this patient has not developed lymphedema despite previous radical pelvic and inguinal lymphadenectomy.

Case II indicates the intimate relationship of the lymphatic and venous systems with utilization of lymphatico-venous anastomoses including the portal system. Direct communication from lymph node to venous system has been demonstrated previously experimentally[7] as well as clinically.[2] However, the demonstration of utilization of the portal system in our series appears unique in reported cases. We have observed this in 2 cases. Both showed severe lymphatic obstruction in the common iliac lymph node region and complete, or almost complete, obstruction of the inferior vena cava on the cavagram.

Case III might have been expected to show contrast material deposition in the liver similar to that in Case II, since severe lymphatic obstruction as well as complete vena cava obstruction was present. Our only explanation is that the relative uptake of contrast material by the tumor mass was so great that only a relatively small amount of contrast material utilized the lymphatico-venous anastomoses. The extensive

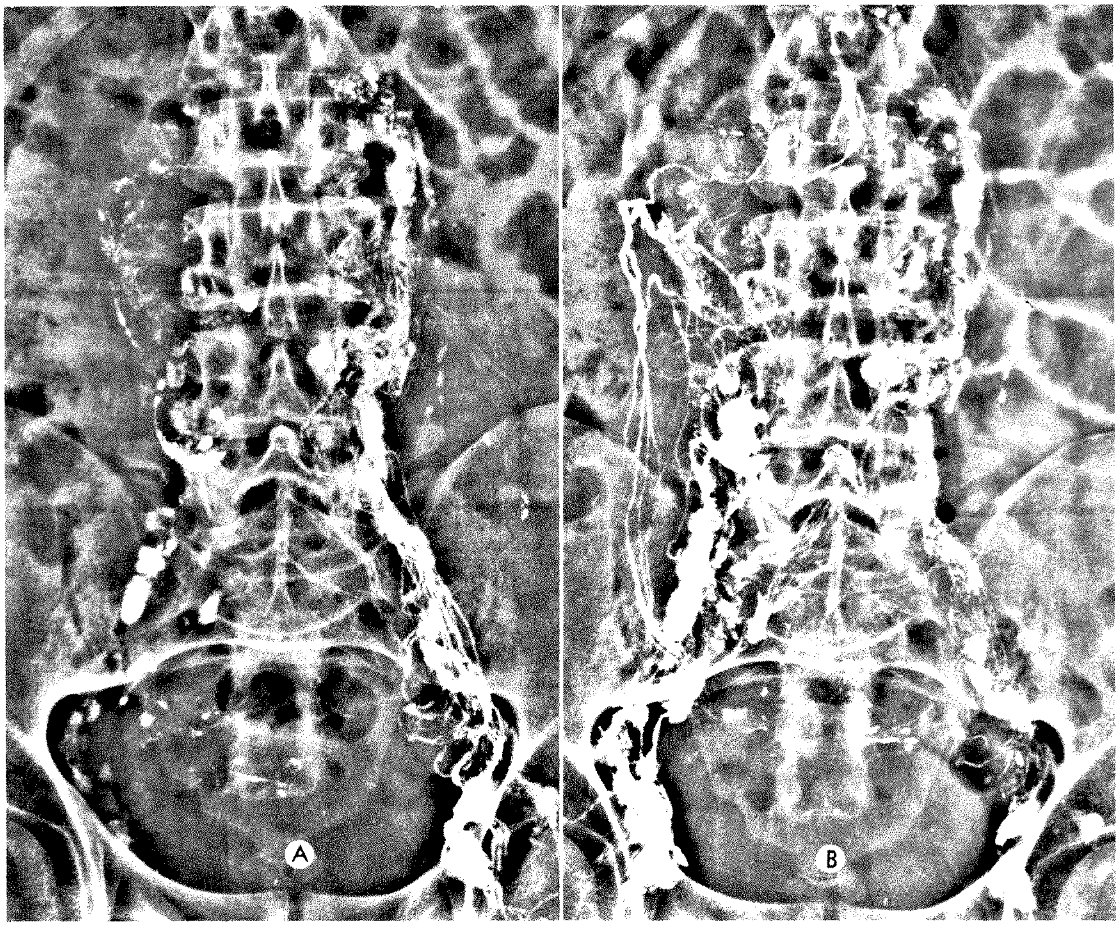


Fig. 8. Case III. (*A* and *B*) "Second-look" lymphograms (during injection) done near the end of therapy which show that extensive collateral lymphatic circulation has developed. There is venous filling seen to the left of the L2–L3 disk space.

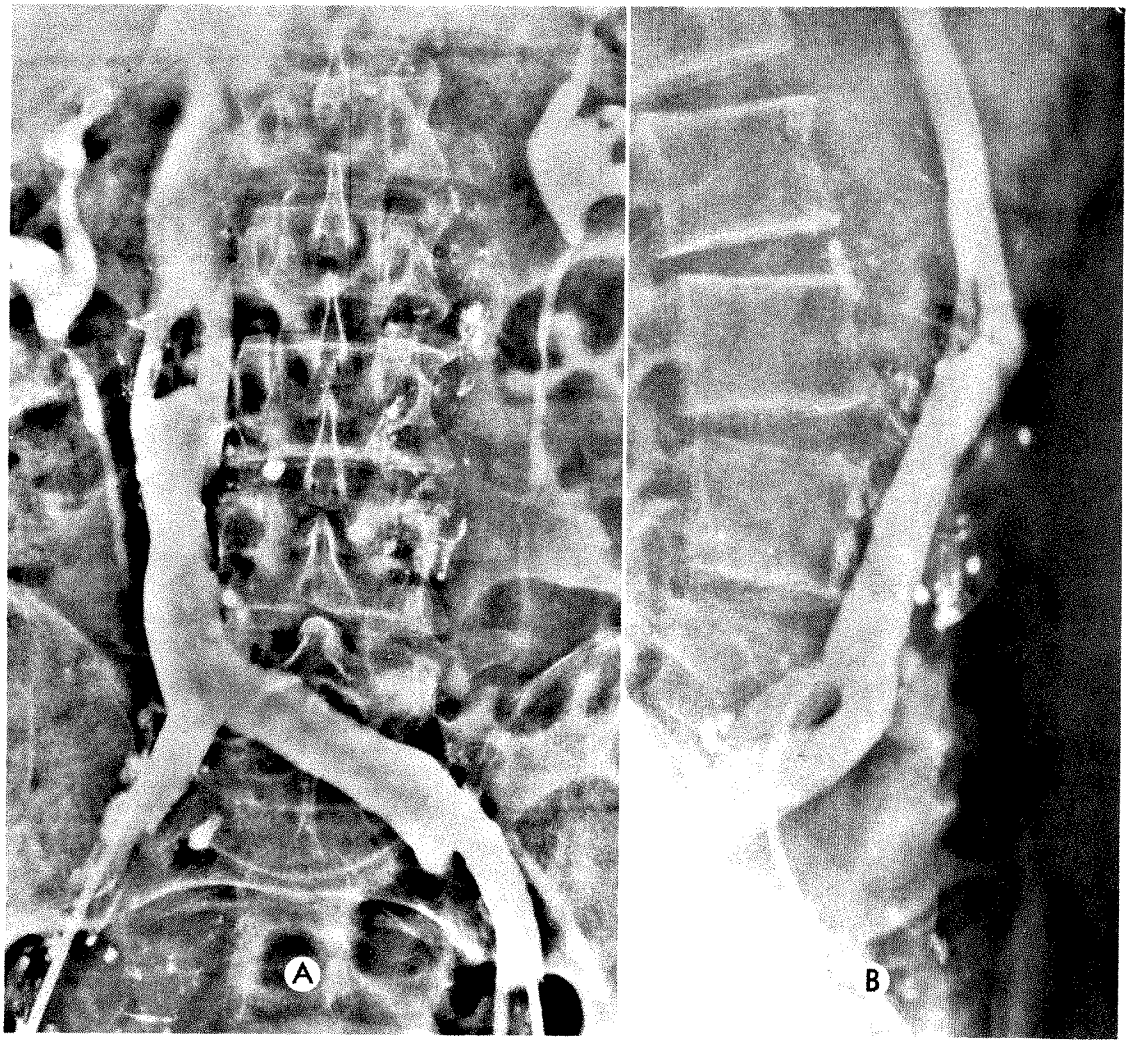


Fig. 9. Case III. (*A* and *B*) Inferior vena cavagrams done at the end of therapy showing free flow with extrinsic defect due to residual mass.

collateral channels seen on the "second-look" lymphogram in this case are most interesting. Although proof is lacking, it is our feeling that these are not new lymphatic trunks that have developed, but that they are relatively little-used normal channels that have become well developed in the presence of proximal obstruction of major pathways. This theory has been proposed by other authors previously.[1]

SUMMARY

The limitations of lymphography by current techniques have been presented. "Second-look" lymphography has not elimiated these limitations, but it has provided an objective means of evaluating the changing status of the lymphatic system in different phases of the course of malignant disease in selected cases.

Lymphatico-venous anastomoses are present normally, but they are predominantly utilized in lymphatic obstruction. Deposition of contrast material in the liver through pelvic lymph node-venous anastomoses to the portal system is described.

This occurred in 2 cases as a result of common iliac lymphatic obstruction and concomitant inferior vena cava and/or common iliac vein obstruction.

John R. Thornbury, M.D.
Department of Radiology
University Hospitals
Iowa City, Iowa

REFERENCES

1. Bower, R., Danese, C., Debbas, J., and Howard, J. M. Advances in diagnosis of diseases of lymphatics. *J.A.M.A.*, 1962, *181*, 687–691.
2. Bron, K. M., Baum, S., and Abrams, H. L. Oil embolism in lymphangiography; incidence, manifestations, and mechanism. *Radiology*, 1963, *80*, 194–202.
3. Fischer, H. W., Lawrence, M. S., and Thornbury, J. R. Lymphography of normal adult male; observations and their relation to diagnosis of metastatic neoplasm. *Radiology*, 1962, *78*, 399–406.
4. Fuchs, W. A., and Böök-Hederström, G. Inguinal and pelvic lymphography; preliminary report. *Acta radiol.*, 1961, *56*, 340–354.
5. Kinmonth, J. B. Lymphangiography in man; method of outlining lymphatic trunks at operation. *Clin. Sc.*, 1952, *11*, 13–20.
6. Kinmonth, J. B., Taylor, G. W., and Kemp Harper, R. A. Lymphangiography; technique for its clinical use in lower limb. *Brit. M. J.*, 1955, *1*, 940–942.
7. Pressman, J. J., Simon, M. B., Hand, K., and Miller, J. Passage of fluids, cells, and bacteria via direct communications between lymph nodes and veins. *Surg., Gynec. & Obst.*, 1962, *115*, 207–214.
8. Sheehan, R., Hreshchyshyn, M., Lin, R. K., and Lessmann, F. P. Use of lymphography as diagnostic method. *Radiology*, 1961, *76*, 47–53.
9. Wallace, S., Jackson, L., Schaffer, B., Gould, J., Greening, R. R., Weiss, A., and Kramer, S. Lymphangiograms: their diagnostic and therapeutic potential. *Radiology*, 1961, *76*, 179–199.

VOL. 90, No. 5

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

Editor: TRAIAN LEUCUTIA, M.D.
Assistant to the Editor: KENNETH L. KRABBENHOFT, M.D.
Associate Editors: HARRY HAUSER, M.D., RUSSELL H. MORGAN, M.D., EDWARD B. D. NEUHAUSER, M.D., WENDELL G. SCOTT, M.D.
Consulting Editorial Board: See front cover.
Published by: CHARLES C THOMAS, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois.

Issued monthly. Annual subscription: United States, Mexico, Cuba, Central and South America, and Canada $15.00; other countries, $17.00. Current single numbers, $1.50. Advertising rates submitted on application. Editorial office, 110 Professional Building, Detroit 1, Michigan. Office of publication, 301–327 East Lawrence Avenue, Springfield, Illinois. Information of interest to authors and readers will be found on page ii.

AMERICAN ROENTGEN RAY SOCIETY

President: E. E. Barth, Chicago, Ill.; *President-Elect:* R. M. Caulk, Washington, D. C.; *1st Vice-President:* A. C. Singleton, Toronto, Ont., Canada; *2nd Vice-President:* G. Cooper, Jr., Charlottesville, Va.; *Secretary:* C. A. Good, Mayo Clinic, Rochester, Minn.; *Treasurer:* S. W. Brown, 1467 Harper Street, Augusta, Ga.

Executive Council: E. E. Barth, R. M. Caulk, A. C. Singleton, C. A. Good, S. W. Brown, W. Bailey, J. F. Roach, L. E. Etter, T. Leucutia, H. G. Reineke, H. O. Peterson, J. C. Cook, J. D. Reeves, H. M. Stauffer, T. F. Leigh, E. L. Pirkey, J. P. Medelman, Chairman, 110 Birchwood Avenue, Birchwood, White Bear Lake 10, Minn.

Program Committee: C. A. Good, Rochester, Minn.; J. F. Roach, Albany, N. Y.; T. Leucutia, Detroit, Mich; L. E. Etter, Pittsburgh, Pa.; J. P. Medelman, White Bear Lake, Minn.; H. O. Peterson, Minneapolis, Minn.; R. M. Caulk, Chairman, Washington, D. C.

Publication Committee: M. M. Figley, Seattle, Wash.; R. N. Cooley, Galveston, Tex; J. F. Holt, Ann Arbor, Mich.; B. R. Young, Philadelphia, Pa.; J. F. Roach, Chairman, Albany, N. Y.

Finance and Budget Committee: T. F. Leigh, Atlanta, Ga.; E. L. Pirkey, Louisville, Ky.; C. B. Holman, Rochester, Minn.; J. A. Campbell, Indianapolis, Ind.; W. Bailey, Chairman, Los Angeles, Calif.

Committee on Scientific Exhibits: R. R. Greening, Philadelphia, Pa.; J. S. Dunbar, Montreal, Que., Canada; L. E. Etter, Chairman, Pittsburgh, Pa.

Representatives on the American Board of Radiology: C. A. Stevenson, Spokane, Wash.; J. F. Roach, Albany, N. Y.; C. A. Good, Rochester, Minn.

Director of Instructional Courses: H. O. Peterson, Minneapolis, Minn.; *Manager of the Annual Meeting:* J. C. Cook, 110 Professional Building, Detroit 1, Mich.

Editor: T. Leucutia, 110 Professional Building, Detroit 1, Mich.

Sixty-fourth Annual Meeting: Queen Elizabeth Hotel, Montreal, Quebec, Canada, October 8–11, 1963.

AMERICAN RADIUM SOCIETY

President: Charles G. Stetson, Tenafly, N. J.; *President-Elect:* Joseph H. Farrow, New York, N. Y.; *1st Vice-President:* Juan A. del Regato, Colorado Springs, Colo.; *2nd Vice-President:* John L. Pool, New York, N. Y.; *Secretary:* Justin J. Stein, Los Angeles, Calif.; *Treasurer:* Milton Friedman, 1016 Fifth Ave, New York 28, N. Y.

Executive Committee: Jesshill Love, Chairman; Robert L. Brown; Gilbert H. Fletcher; Charles G. Stetson; Justin J. Stein; Joseph H. Farrow; Juan A. del Regato; John L. Pool; Milton Friedman.

Scientific Program Committee: Charles G. Stetson, Chairman; A. N. Arneson, St. Louis, Mo.; Milton Friedman, New York, N. Y.; Harold E. Johns, Toronto, Ont.; Henry S. Kaplan, Palo Alto, Calif.; Calvin T. Klopp, Washington, D. C.; Milford D. Schulz, Boston, Mass.; Joseph H. Farrow, Ex officio.

Committee on Arrangements: Henri LeClaire, Chairman, Cincinnati, Ohio; Manuel Garcia, Chairman Designate, New Orleans, La.; Albert L. Allen, Huntington, W. Va.; Robert D. Berkebile, Elyria Ohio; H. Peter Mueller, Belmont, Mass.; Ralph M. Scott, Louisville, Ky.; Milton Friedman, Ex officio.

Publication Committee: Harry Hauser, Chairman, Cleveland, Ohio; Wendell C. Hall, Hartford, Conn.; Martin Van Herik, Rochester, Minn.

Public Relations Committee: H. Peter Mueller, Chairman, Belmont, Mass.; Harold W. Jacox, New York, N. Y.; Charles H. Peterson, Roanoke, Va.

Janeway Lecture Committee: Edith H. Quimby, Chairman, New York, N. Y.; William S. MacComb, Houston, Tex.; Clifford L. Ash, Toronto, Ont.

Representatives on the American Board of Radiology: Frederick W. O'Brien, Boston, Mass.; Bernard P. Widmann, Philadelphia, Pa.; Donald S. Childs, Jr., Rochester, Minn.

Representatives on the National Committee on Radiation Protection: Robert Robbins, Philadelphia, Pa.; Herbert M. Parker, Richland, Wash.

Representative on the Board of Chancellors of the American College of Radiology: Milford D. Schulz.

Forty-sixth Annual Meeting: Greenbrier Hotel, White Sulphur Springs, W. Va., April 13–16, 1964.

EDITORIAL

COMPUTERS IN DOSIMETRY*

THE possibility of utilizing high-speed digital computers in routine radiation dosimetry has raised hopes that some or all of the drudgery of repeated calculations can be removed from the planning of radiation treatments. The pioneer work with computers in radiotherapy was done almost 10 years ago by Tsien[1] and Laughlin, and it is now appropriate to evaluate past experience with computers and to anticipate the magnitude of future use in this area. The views expressed here are shared by a number of radiation physicists, but not by all.

Computer methods find their best application in those areas in which the methods provide new and useful clinical information which is not available by usual manual methods. For example, the availability of full isodose distributions for individual patients in radium needle implants,[2,3] in iridium seed implants,[4] and in intracavitary radium treatment of carcinoma of the cervix[5] reveals the radiation distribution in its complexity for use in medical decisions such as the alteration of the treatment geometry or the determination of treatment time. For 30 years, the radiotherapist has based interstitial and intracavitary treatments upon a single dose rate calculated from tables and has achieved notable success with this limited information. It is too soon to say with certainty that the greater amount of dosimetric information made available by the computer will improve cure rates; however, a retrospective analysis by computer of cases treated by radium needles reveals a correlation between necrosis and high local dose and between recurrence and low local dose.[6] Thus it is likely that the new information will result in improved cure rates and a lowered incidence of necrosis.

A second class of computer use in radiotherapy includes those applications which produce the same information as manual methods but with greater speed and less human effort. The gains and losses in adopting an automatic method need careful evaluation in these cases. In general, 6 man-months of programming and testing may be required before a computer program produces a result that is acceptable for routine clinical use. In addition, with machine calculation there is a loss of direct contact between the individual and the final calculation, which makes errors more difficult to detect and reduces the teaching value of individual patient problems—particularly for those students who will not have machines available later. For example, in the writer's opinion, the calculation of isodose distributions in individual cases for multiport, stationary radiation fields is better done by manual graphical methods than by automatic means. In most anatomic sites the treatments become stylized and the dosimetry can be reduced to dosage tables and atlases of dose distribution which are applicable to individual patients. If a full distribution is required, a skilled technician needs about one-half hour for the calculation—probably not much longer than the preparation of the data for machine input, calculation, and analysis of the result. However, for devising or optimizing systems of fixed-beam dosimetry in a general way, the saving of time by the computer might be very significant.[7] An example of a problem that may merit computer calculation is that of rotational radiation distributions. If an institution has had sufficient experience with this modality of treatment to have atlases of dose patterns and tables of doses, a computer method is clearly not indicated. However, if each patient plan on rotational therapy is calculated in full, as it is at this institution, the 1½ to 2 hours required by manual calculation is laborious and discourages optimization and trial calculations; thus, the initial effort required for a machine method of rotational calculation might be justified. At this institution the present plans are to continue with the routine use of computers for isodose curves in implants, to complete development of a similar system for intracavitary cervix treatment, to consider further the practicality of rotational calculations by computer, and in the isotope area to consider the possibility of delineating in three dimensions the location and concentration of radioactive material within the body from scanning data.

---

[1] TSIEN, K. C. Application of automatic computing machines to radiation treatment planning. *Brit. J. Radiol.*, 1955, *28*, 432–439.

[2] SHALEK, R. J., and STOVALL, M. A. Calculation of isodose distributions in interstitial implantations by computer. *Radiology*, 1961, *76*, 119–120.

[3] STOVALL, M. A., and SHALEK, R. J. Study of explicit distribution of radiation in interstitial implantations. I. Method of calculation with automatic digital computer. *Radiology*, 1962, *78*, 950–954.

[4] LAUGHLIN, J. S., SILER, W. M., HOLODNY, E. I., and RITTER, F. W. Dose description system for interstitial radiation therapy; seed implants. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1963, *89*, 470–490.

[5] MEURK, M. L., and ADAMS, G. D. Computer evaluation of dose rates around multiple radium sources. *Radiology*, 1963, *80*, 115–116.

[6] FLETCHER, G. H., and STOVALL, M. A. Study of explicit distribution of radiation in interstitial implantations. II. Correlation with clinical results in squamous cell carcinomas of anterior two-thirds of tongue and floor of mouth. *Radiology*, 1962, *78*, 766–782.

* This investigation was supported in part by U. S. Public Health Service Research Grant CA 06294 from the National Cancer Institute.

For dosimetric purposes, large digital computers with magnetic tape input-output, such as the IBM 709 and the CDC 1604, are the most useful although medium-sized computers, such as the IBM 1620, have been used. If paid for on a commercial basis, the cost for calculation of the isodose distribution for an average interstitial implant is $20 to $40; other dosimetric calculations would require about the same amount of computer time.

It would be unfortunate if the view became prevalent that the quality of radiotherapy at an institution is dependent upon the possession of a computer. At this time there is indication that dosimetry by computer might improve the clinical results in interstitial radiation treatment; however, such cases constitute only a small fraction of the total treated by radiation, and if a computer is not available locally, input data may be transmitted to computing centers by telephone and output data returned by air mail. In external beam treatments, new information on individual cases has not been made available by computer methods and the quality of treatment has not been affected. On the other hand, if in the treatment of carcinoma of the cervix it can be demonstrated that dosimetry with a computer improves the clinical result, then the availability and proximity of a machine would influence the quality of treatment since the short treatment times make long distance communication impractical without special teleprocessing units. However, it will be some few years before this last question can be answered.

In summary, the use of computers in radiation dosimetry is a highly interesting development that merits the continued attention of radiologists. At this time, it cannot be demonstrated that the quality of radiotherapy is dependent upon the local availability of a computer, although a future dependence is possible.

Robert J. Shalek, Ph.D.

Department of Physics
The University of Texas
M. D. Anderson Hospital
and Tumor Institute
Houston, Texas

---

[7] Sterling, T. D., Perry, H., and Weinkam, J. J. Automation of radiation treatment planning. III. Simplified system of digitising isodoses and direct print-out dose distribution. *Brit. J. Radiol.*, 1963, *36*, 522–527.

NEWS ITEMS

THE CANADIAN ASSOCIATION OF RADIOLOGISTS

The Twenty-seventh Annual Meeting of The Canadian Association of Radiologists will be held at the Hotel Vancouver, Vancouver, B. C., February 29 to March 4, 1964 (the scientific sessions will commence March 2nd).

The officers are: *President*, W. L. Sloan, M.D.; *Vice-President*, R. A. Lobb, M.D.; *Honorary Secretary-Treasurer*, D. J. Sieniewicz, M.D.; and *Associate Honorary Secretary-Treasurer*, Maurice Dufresne, M.D.

For further information please write to: Dr. D. J. Sieniewicz, Suite 511, 1555 Summerhill Ave., Montreal 25, Quebec, Canada.

III CONGRESO NACIONAL DE RADIOLOGIA

The Third National Congress of Radiology of México will be held in Monterrey, Nuevo León, México, April 12–17, 1964.

The Committee on Arrangements is composed of: *President*, Dr. Espiridion Villarreal; *General Secretary*, Dr. José Hugo Arredondo; *Treasurer*, Dr. Enrique Gonzalez Landois; and other officers of the Congress.

All radiologists of North America are cordially invited to attend.

For further information please contact Dr. Juan M. Henares, Secretary to Foreign Countries, E. Carranza Norte 155, Monterrey, N. L. México.

SIXTEENTH ANNUAL MIDWINTER RADIOLOGICAL CONFERENCE

The Sixteenth Annual Midwinter Radiological Conference, sponsored by the Los Angeles Radiological Society, will be held at the Biltmore Hotel, Los Angeles, California, on Saturday and Sunday, February 1 and 2, 1964.

An outstanding program has been arranged, the guest speakers including: Ernest E. Aegerter, M.D., Philadelphia, Pa.; A. N. Arneson, M.D., St. Louis, Mo.; Roy Astley, M.D., The Children's Hospital, Birmingham, England; Gwilym S. Lodwick, M.D., Columbia, Mo.; and Hal Luke, F.F.R., Alfred Hospital, Victoria, Australia.

For further information please contact Dr. Richard P. Storrs, Secretary-Treasurer, St. Vincent's Hospital, Los Angeles 57, California.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS

At the Annual Meeting of the Association of University Radiologists held at Yale University in New Haven on May 24 and 25, 1963, the following officers were elected: *President*, Herbert M. Stauffer, M.D., *President-Elect*, John A. Campbell, M.D., and *Secretary-Treasurer*, Sidney W. Nelson, M.D.

The winner of the Annual Memorial Medal Award was Harold L. Kundel, M.D., Department of Radiology, Temple University School of Medicine, Philadelphia, Pennsylvania, whose paper was titled, "Osteolathyrism in the Rat."

Next year's meeting of the Association will be held at the University of Chicago School of Medicine, Chicago, Illinois, May 14, 15, and 16, 1964.

An Annual Memorial Medal Award, in honor of deceased AUR members, is awarded to the resident in radiology writing the best original paper on some aspect of radiology during the period of competition. The paper must be the work of only one author, the resident.

The requirements for the papers submitted are: Twenty minutes is the length of time provided for the presentation of the paper. The original paper should run no more than 6,000 words. Illustrations and tables should be kept within reasonable bounds, as the number which can be published without cost to the author is usually limited to less than ten. The length of the paper should be decreased by 100 words for each single illustration and 200 words for each double illustration (*i.e.*, *A* and *B* of a single figure would be equivalent to 200 words). Each full page of illustrations should be equal to about 500 words; thus, if the applicant has 10 illustrations on 5 figures, he should have approximately 5,000 words of text. The author's name should not appear on the manuscript pages.

The applicants should submit 3 copies of their complete papers before the deadline of March 1, 1964, to Dr. Sidney W. Nelson, Secretary-Treasurer, Department of Radiology, Ohio State University Medical Center, 410 W. 10th Avenue, Columbus 10, Ohio.

EIGHTEENTH ANNUAL SYMPOSIUM ON FUNDAMENTAL CANCER RESEARCH

CELLULAR RADIATION BIOLOGY

A symposium considering radiation effects in the cell and possible implications for cancer therapy will be held, March 2, 3, and 4, 1964, at The Shamrock Hilton Hotel, Houston, Texas, under the auspices of The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston 25, Texas.

The subjects discussed will include: (1) Radiation effects on macromolecules; (2) radiation effects on replication of cellular structures; (3) the critical structures in radiation phenomena; (4) modification of radiation response; (5) radiosensitivity in the replication cycle of cells and the relation to fractionation in radiotherapy; and (6) responses in mammalian cells and their implications for radiotherapy of cancer.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

The Year Book of Radiology (1962–1963 Series). Radiologic Diagnosis edited by J. F. Holt, M.D., Professor, Dept. of Radiology, University of Michigan, and W. M. Whitehouse, M.D., Associate Professor, Dept. of Radiology, University of Michigan; Radiation Therapy edited by H. W. Jacox, M.D., Professor of Radiology, College of Physicians and Surgeons, Columbia University, and M. M. Kligerman, M.D., Professor of Radiology and Chairman of the Dept. of Radiology, Yale University School of Medicine. Cloth. Price, $11.75. Pp. 435 with 334 illustrations. Chicago, Year Book Publishers, Inc., 1963.

A tradition of excellence has been established over many years for the Yearbook of Radiology. Anyone unfamiliar with this annual volume would do well to procure it in order to keep abreast of recent advances in diagnostic and therapeutic radiology and nuclear medicine. Pertinent articles have been painstakingly selected and abstracted from all sources of world medical literature. Candid and informative editorial comments are liberally used, and hundreds of quality illustrations make this a text that is difficult to lay aside.

The editors comment on the increasing complexity and technological advances in x-ray equipment coming into general use which afford newer and more accurate methods of diagnosis. There is hardly an organ or a vascular or lymphatic system in the body which has not yet been investigated with new techniques. In radiation therapy there has been a steady advancement in accumulated knowledge and many articles with large series of cases have been abstracted, both from American and Foreign Journals.

Arch H. Hall, M.D.

Tumors of the Eye. Second Edition. By Algernon B. Reese, M.D., D.Sc. (Hon.), M.D. (Hon.), LL.D. (Hon.), Consulting Ophthalmologist and Pathologist, Institute of Ophthalmology; Clinical Professor of Ophthalmology, Emeritus, College of Physicians and Surgeons, Columbia University, New York City. Cloth. Pp. 593, with 734 illustrations. Price, $30.00. Hoeber Medical Division, Harper & Row, Publishers, New York, 1963.

The second edition, Tumors of the Eye, should be considered a standard textbook for students in ophthalmology, pathology, and radiology. The book is comprehensive as well as beautifully illustrated and well worth the purchase price.

Several sections are of particular interest; namely, the section on retinoblastoma—Dr. Reese's personal experience with retinoblastoma is not matched in medical history. The section on pigmentary tumors brings forth many of the problems of these peculiar lesions and should prove of immeasurable aid to anyone who must deal with melanomas. The other sections of the book are likewise most instructive because they are all encompassing.

The entire book has unusual value; it is a classic of its kind.

A. D. Ruedemann, Jr., M.D.

BOOKS RECEIVED

The Year Book of Cancer (1962–1963 Year Book Series). Edited by Randolph Lee Clark, B.S., M.D., M.Sc., D.Sc., Director and Surgeon-in-Chief, The University of Texas M. D. Anderson Hospital and Tumor Institute; Professor of Surgery, The University of Texas Postgraduate School of Medicine; Clinical Professor of Surgery, Baylor University College of Medicine; Chairman, Committee on Cancer, American College of Surgeons (F.A.C.S.); and Russell W. Cumley, B.A., M.A., Ph.D., Director of Publications, The University of Texas M. D. Anderson Hospital and Tumor Institute; Professor of Medical Journalism, The University of Texas Postgraduate School of Medicine; Executive Editor, Medical Arts Publishing Foundation. Cloth. Pp. 524, with 214 illustrations. Price, $8.50. Year Book Medical Publishers, Inc., 35 E. Wacker Drive, Chicago 1, Ill., 1963.

Early Cancer: Prevention, Detection, Course, Treatment. By Leonard B. Goldman, M.D., Chairman, Tumor Conference and Director, Radiation Medicine Department, Queens Hospital Center; Consultant Radiation Therapist, Flushing, Booth Memorial, St. Joseph's (Far Rockaway), South Nassau Communities and Peninsula General Hospitals, New York. Formerly, Clinical Professor of Radiotherapy, New York Medical College, Flower and Fifth Avenue Hospitals. Cloth. Pp. 324, with many illustrations. Price, $12.50. Grune & Stratton, Inc., 381 Park Avenue South, New York 16, New York, 1963.

ENCYCLOPEDIA OF X-RAYS AND GAMMA RAYS. Edited by George L. Clark, Research Professor of Analytical Chemistry, Emeritus, University of Illinois, Urbana, Illinois. Cloth. Pp. 1,149, with many illustrations. Price, $35.00. Reinhold Publishing Corporation, 430 Park Avenue, New York 22, New York, 1963.

RADIOISOTOPES AND IONIZING RADIATIONS IN ENTOMOLOGY. BIBLIOGRAPHICAL SERIES. No. 9. Sponsored by the International Atomic Energy Agency, Vienna, 1963. Paper. Pp. 414. Price, $6.50. International Publications, Inc., and Unesco Publications Center, 317 East 34th Street, New York 16, New York, 1963.

THE ELECTROCARDIOGRAM AND CHEST X-RAY IN DISEASES OF THE HEART. By Arthur M. Master, M.D., Consultant Cardiologist, The Mt. Sinai Hospital, New York City, The U. S. Marine Hospital, Staten Island, New York, The Englewood Hospital, Englewood, New Jersey, and The Beth-El Hospital, Brooklyn, New York; Richard P. Lasser, M.D., Assistant Attending Physician for Cardiology, The Mt. Sinai Hospital, New York City; Isadore Rosenfeld, M.D., Instructor in Medicine, Cornell University Medical College, New York City; and Ephraim Donoso, M.D., Assistant Attending Physician for Cardiology, The Mt. Sinai Hospital, New York City. Cloth. Pp. 565, with 376 illustrations. Price, $21.00. Lea & Febiger, 600 Washington Square, Philadelphia, Pa., 1963.

GENETICALLY SIGNIFICANT RADIATION DOSES IN DIAGNOSTIC RADIOLOGY. By Erling Hammer-Jacobsen, M.D. Supplementum 222 to *Acta radiol.*, Stockholm 2, Sweden. Paper. Pp. 277. Price Sw. Kr. 35:–, 1963.

pH AND DISSOCIATION. A LEARNING PROGRAM FOR STUDENTS OF THE BIOLOGICAL AND MEDICAL SCIENCES. By Halvor N. Christensen, Ph.D., Professor of Biological Chemistry and Chairman of the Department, University of Michigan. Paper. Pp. 60. Price, $1.75. W. B. Saunders Company, Philadelphia, Pa., 1963.

ACTUALITÉS SUR LES TUMEURS CUTANÉES. Service du Professeur Agrégé Duperrat, Hôpital Saint-Louis, Paris. Paper. L'Expansion Scientifique Française, 15, Rue Saint-Benoit, Paris 6e, France, 1963.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

United States of America

American Roentgen Ray Society

Secretary, Dr. C. Allen Good, Mayo Clinic, Rochester, Minn. Annual meeting: Queen Elizabeth Hotel, Montreal, Que., Canada, Oct. 8–11, 1963.

American Radium Society

Secretary, Dr. Justin J. Stein, U.C.L.A. Medical Center, Los Angeles 24, Calif. Annual meeting: Greenbrier Hotel, White Sulphur Springs, W. Va., April 13–16, 1964.

Radiological Society of North America

Secretary, Maurice Doyle Frazer, 1744 South Fifty-eighth St., Lincoln, Neb.

Treasurer, Dwight Vincent Needham, 713 E. Genessee St., Syracuse, N. Y. Annual meeting: Palmer House, Chicago, Ill., Nov. 17–22, 1963.

American College of Radiology

Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Ill. Annual meeting: Ramada Inn, Tucson, Ariz., Feb. 5–8, 1964.

Section on Radiology, American Medical Association

Secretary, Dr. Clyde A. Stevenson, Sacred Heart Hospital, West 101 Eighth Ave., Spokane 4, Wash. Annual meeting: San Francisco, Calif., June 21–25, 1964.

American Board of Radiology

Secretary, Dr. H. Dabney Kerr. Correspondence should be directed to Kahler Hotel Building, Rochester, Minn. The Fall 1963 examination will be held at the Terrace Hilton Hotel, Cincinnati, Ohio, December 2–6, inclusive. Deadline for filing applications was June 30, 1963. The Spring 1964 examination will be held at the Americana Hotel, New York City, June 8–12, inclusive. Deadline for filing applications is December 31, 1963. There will be a Special Examination in Nuclear Medicine for diplomates in Radiology or Therapeutic Radiology if sufficient applications are received. The Fall 1964 examination will be held at the Americana Hotel, Bal Harbour, Florida, December 7–11, inclusive. Deadline for filing applications is June 30, 1964.

American Association of Physicists in Medicine

Secretary-Treasurer, Charles S. Simons, University of Michigan Hospital, Ann Arbor, Mich. Annual meeting to be announced.

American Club of Therapeutic Radiologists

Secretary, Dr. J. A. del Regato, Penrose Cancer Hospital, Colorado Springs, Colo.

Eleventh International Congress of Radiology

Secretary-General, Professor Dr. Med. Arduino Ratti, via Moscova, 44-1, Milan, Italy. Address inquiries to Professor Dr. Med. Luigi Turano, President-Elect, Istituto di Radiologia, Università di Roma, Rome, Italy. Meeting: September 22–28, 1965.

Eighth Inter-American Congress of Radiology

Counselor for the United States, Dr. Philip J. Hodes, Jefferson Medical College Hospital, 11th and Walnut Streets, Philadelphia 7, Pennsylvania.

Secretary, Dr. Mario Gaitan-Yanguas, Bogotá, Colombia. Meeting to be announced.

Alabama Radiological Society

Secretary, Dr. Walter Brower, Birmingham, Ala. Meets time and place of Alabama State Medical Association.

American Nuclear Society

Treasurer, Raymond Maxson, 86 E. Randolph St., Chicago, Ill. Annual meeting to be announced.

Arizona Radiological Society

Secretary-Treasurer, Dr. E. Lawrence Ganter, 1820 E. Polk St., Phoenix 34, Ariz. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society

Secretary, Dr. Charles W. Anderson, 1108½ Poplar, Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Association of University Radiologists

Secretary-Treasurer, Dr. Sidney W. Nelson. Annual Meeting: University of Chicago School of Medicine, Chicago, Illinois, May 14–16, 1964.

Atlanta Radiological Society

Secretary, Dr. Donald R. Rooney, Burnt Hickory Road, Marietta, Ga. Meets monthly except during three summer months, on third Tuesday, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

Bavarian-American Radiologic Society

Secretary, Dr. Robert W. Edland, Major MC USA, United States Army Hospital Augsburg, 21st Evacuation Hospital, Chief of Radiology Service, APO 178, New York, N. Y. Meets quarterly.

Blockley Radiological Society

Secretary, Dr. Bernard J. Ostrum, 2412 North 52nd St., Philadelphia, Pa.

Brooklyn Radiological Society

Secretary, Dr. Peter J. Lampros, 121 Dekalb Ave., Brooklyn, N. Y. Meets first Thursday of each month October through May.

Buffalo Radiological Society

Secretary, Dr. Eugene V. Leslie, Edward J. Beyer Memorial Hosp., Buffalo 15, N. Y. Meets second Monday evening each month, October to May inclusive.

California Radiological Society

Secretary, Dr. L. Henry Garland, Suite 1739, 450 Sutter St., San Francisco, Cal. Meets annually during meeting of California Medical Association.

Central New York Radiological Society

Secretary Dr. Edward W. Carsky, Crouse-Irving Hospital, 820 S. Crouse Ave., Syracuse, N. Y. Meets first Monday each month October through May.

Central Ohio Radiological Society

Secretary-Treasurer, Dr. Harold W. Long, 81 S. Fifth St., Columbus 15, Ohio. Meets third Thursday in October, and second Thursday in November, January, March, and May at Fort Hayes Hotel, Columbus, Ohio.

Central Society of Nuclear Medicine

Secretary, Dr. Robert S. Landauer, Radiation Center Bldg., 1903 West Harrison St., Chicago 12, Ill.

Chicago Roentgen Society

Secretary, Dr. Abram H. Cannon, 250 E. Superior St., Chicago 11, Ill. Meets second Thursday of each month, October to April except December at the Pick-Congress Hotel at 8:00 P.M.

Cleveland Radiological Society

Secretary-Treasurer, Dr. James Christie, 10515 Carnegie Avenue, Cleveland, Ohio. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

Colorado Radiological Society

Secretary, Dr. Seward Imes, 1845 High St., Denver, Colo. Meets third Friday of each month at Denver Athletic Club from September through May.

Connecticut Valley Radiologic Society

Secretary, Dr. James L. Krieger, 85 Jefferson St., Hartford 6, Conn. Meets first Friday in February and April.

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Dallas-Fort Worth Radiological Society

Secretary, Dr. Robert D. Moreton, 816 Medical Arts Bldg., Fort Worth, Tex. Meets monthly, third Monday, at Greater Fort Worth International Airport at 6:30 P.M.

Detroit Roentgen Ray and Radium Society

Secretary, Dr. Arch H. Hall, Harper Hospital, Detroit 1, Mich. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

East Bay Roentgen Society

Secretary, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland, Calif.

East Tennessee Radiological Society

Secretary, Dr. J. Marsh Frere, Jr., 205 Medical Arts Bldg., Knoxville, Tenn. Meets in January and September.

Eastern Conference of Radiologists

Secretary, Arrangements Committee, Dr. Theodore A. Tristan, 3400 Spruce St., Philadelphia 4, Pa. Annual meeting to be announced.

Eastern Radiological Society

Secretary, Dr. James F. Martin, North Carolina Baptist Hospital, Winston-Salem, N. C.

Florida Radiological Society

Secretary, Dr. David Kirsh, 712 Du Pont Bldg., Miami, Fla. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

Florida West Coast Radiological Society

Secretary-Treasurer, Dr. Garth R. Drewry, Tampa General Hospital, Tampa 6, Fla. Meets in January, April, July and October.

Georgia Radiological Society

Secretary, Dr. David Robinson, P.O. Box 394, Savannah, Ga. Meets in spring and fall with Annual State Society Meeting.

Greater Miami Radiological Society

Secretary, Dr. Robert F. Feltman, Dade County Medical Association Building, Two S.E. Thirteenth St., Miami 32, Fla. Meets monthly, third Wednesday at 8:00 P.M. at Jackson Memorial Hospital, Miami, Fla.

Greater St. Louis Society of Radiologists

Secretary, Dr. C. M. Witt, #16 Hampton Village Plaza, St. Louis 9, Mo.

Houston Radiological Society

Secretary, Dr. W. A. Goodrich, Jr., Texas Medical Center Library, Jesse H. Jones Library Bldg., Houston 25, Tex. Meets fourth Monday of each month, except June, July, August and December, at the Doctors' Club, 8:00 P.M., Houston, Tex.

Idaho State Radiological Society

Secretary, Dr. George H. Harris, Bannock Memorial Hospital, Pocatello, Idaho. Meets in the spring and fall.

Illinois Radiological Society

Secretary, Dr. George A. Miller, Carle Hospital Clinic, Urbana, Ill. Meets in the spring and fall.

Indiana Roentgen Society, Inc.

Secretary, Dr. Richard A. Silver, 1815 N. Capitol Avenue, Indianapolis, Ind. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society

Secretary, Dr. L. L. Maher, 1419 Woodland Ave., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society

Secretary, Dr. Roger K. Wallace, Riley County Hospital, Manhattan, Kan. Meets in spring with State Medical Society and in winter on call.

Kentucky Radiological Society

Secretary, Dr. Lawrence A. Davis, 226 East Chestnut St., Louisville, Ky. Meets monthly on second Friday at Sheraton Hotel, Louisville.

Kings County Radiological Society

Secretary, Dr. Abraham Berens, 1917 Bedford Ave., Brooklyn 25, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Knoxville Radiological Society

Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

Los Angeles Radiological Society

Secretary, Dr. Bernard J. O'Loughlin, Dept. of Radiology, UCLA Center for Health Sciences, Los Angeles 24, Calif. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles.

Maine Radiological Society

Secretary, Dr. Charles W. Capron, Maine Medical Center, Portland, Me. Meets in June, September, December and April.

Maryland Radiological Society

Secretary, Dr. Henry Startzman, Medical Arts Building, Baltimore, Maryland.

Memphis Roentgen Society

Secretary-Treasurer, Dr. Irving K. Ettman, 684 W. Brookhaven Circle, Memphis, Tenn. Meets first Monday of each month at John Gaston Hospital.

Miami Valley Radiological Society

Secretary, Dr. William D. Roberts, 2197 Los Arrow Dr., Dayton 9, Ohio. Meets second Friday of fall and winter months.

Mid-Hudson Radiological Society

Secretary, Dr. Joseph Sorrentino, St. Francis Hospital, Poughkeepsie, N. Y. Meets 8:30 P.M., fourth Wednesday of each month September to May.

Milwaukee Roentgen Ray Society

Secretary-Treasurer, Dr. Harold F. Ibach, 2400 W. Villard Avenue, Milwaukee 9, Wis. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society

Secretary-Treasurer, Dr. Frank J. Anderson, 810 E. 27th St., Minneapolis 7, Minn. Meets three times annually, in fall, winter and spring.

Mississippi Radiological Society

Secretary, Dr. Jack K. Goodrich, University Medical Center, Jackson, Miss. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

Montana Radiological Society

Secretary, Dr. John M. Fritts, 1224 S. Higgins Ave., Missoula, Montana. Meets at least once a year.

Nassau Radiological Society

Secretary, Dr. Herbert Kantor, 71 S. Oyster Bay Rd., Syosset, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

Nebraska State Radiological Society

Secretary, Dr. Richard Bunting, The Radiologic Center, Nebraska Methodist Hospital, Omaha 31, Neb. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

Nevada Radiological Society

Secretary, Dr. William G. Arbonies, Department of Radiology, St. Mary's Hospital, Reno, Nev.

New England Roentgen Ray Society

Secretary, Dr. Robert E. Wise, 605 Commonwealth Ave., Boston 15, Mass. Meets third Friday of each month, October through April, at The Longwood Towers, 20 Chapel Street, Brookline, Mass. at 4:30 P.M.

New Hampshire Roentgen Ray Society

Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly.

New Mexico Association of Radiologists.

Secretary-Treasurer, Dr. Justin J. Wolfson, Department of Radiology, Bernalillo County-Indian Hospital, Albuquerque, New Mexico.

New York Roentgen Society
Secretary, Dr. James J. Nickson, Memorial Hospital, New York, N. Y. Meets monthly on third Monday at the New York Academy of Medicine at 4:30 P.M.

North Carolina Radiological Society
Secretary, Dr. Simmons J. Patrick, Lenoir Memorial Hospital, Kinston, N. C. Meets in the spring and fall each year.

North Dakota Radiological Society
Secretary, Dr. John Jestadt, Depuy-Sorkness Clinic, Jamestown, N. D. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. Charles H. Newell, 800 Miami Road, Jacksonville 7, Fla. Meets quarterly in March, June, September and December.

Northeastern New York Radiological Society
Secretary, Dr. Anthony J. Tabacco, 621 Central Ave., Albany 6, N. Y. Meets in Albany area on second Wednesday of October, November, March and April.

Northern California Radiological Society
Secretary, Dr. Rob H. Kirkpatrick, 1219 28th St., Sacramento, Calif. Meets at dinner last Monday of each month, September to June.

Northwestern Ohio Radiological Society
Secretary, Dr. Anthony F. Lalli, 421 Michigan St., Toledo, Ohio.

Ohio State Radiological Society
Secretary, Dr. M. M. Thompson, Jr., 316 Michigan St., Toledo 2, Ohio. Annual meeting: Cleveland, Ohio, May 23–24, 1964.

Oklahoma State Radiological Society
Secretary, Dr. Simon Pollack, Utica Square Medical Center, Tulsa, Okla. Meets in January, May and October.

Orange County Radiological Society
Secretary-Treasurer, Dr. E. Nicholas Sargent, Orange County General Hospital, Orange, Calif. Meets fourth Tuesday of month except June, July, August and December in Orange County Medical Association Building.

Oregon Radiological Society
Secretary-Treasurer, Dr. James A. Schneider, St. Vincent Hospital, Portland 10, Ore. Meets on second Wednesday of month at 7:00 P.M. at the University Club, Portland, Ore.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets second Tuesday of each month.

Pacific Northwest Radiological Society
Secretary, Dr. Charles E. Donley, 543 East 4th Street, Bend, Ore. Annual meeting on the second weekend in May, 1964.

Pennsylvania Radiological Society
Secretary-Treasurer, Dr. Frederick R. Gilmore, Clearfield Hospital, Clearfield, Pa. Annual meeting: Buckhill Falls, May 21–23, 1964.

Philadelphia Roentgen Ray Society
Secretary, Dr. Antolin Raventos, Hospital of the University of Pennsylvania, Philadelphia 4, Pa. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Marvin Brodie, 3459 Fifth Ave., Pittsburgh 13, Pa. Meets second Wednesday of month, October through June at Park Schenely Restaurant.

Radiological Society of Connecticut
Secretary-Treasurer, Dr. Orlando F. Gabriele, 1450 Chapel St., New Haven 11, Conn. Meetings are held bimonthly.

Radiological Society of Greater Cincinnati
Secretary, Dr. Richard B. Mulvey, 2421 Auburn Ave., Cincinnati, Ohio. Meets first Monday of each month at Cincinnati Academy of Medicine.

Radiological Society of Hawaii
Secretary, Major Carl W. Boyer, Jr., U. S. Army Tripler General Hospital, Honolulu, Hawaii. Meets third Monday of each month at 7:30 P.M.

Radiological Society of Greater Kansas City
Secretary, Dr. J. Stewart Whitmore, 1010 Rialto Bldg., Kansas City, Mo. Meets last Friday of each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of Louisiana
Secretary, Dr. Andrew F. Giesen, Ochsner Clinic, New Orleans 15, La. Meets annually during Louisiana State Medical Society meeting.

Radiological Society of New Jersey
Secretary, Dr. E. Arthur Kratzman, 912 Prospect Ave., Plainfield, N. J. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

Radiological Society of the State of New York
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester 18, N. Y. Annual meeting to be announced.

Radiological Society of South Dakota
Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

Radiological Society of Southern California
Secretary-Treasurer, Dr. Charles G. Campbell, La Jolla, Calif.

Redwood Empire Radiological Society
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma Calif. Meets second Monday every other month.

Richmond County Radiological Society
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, August, Ga. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Gerald R. Holzwasser, Rochester General Hospital, Northside Division, 1425 Portland Ave., Rochester 21, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. John H. Freed, 4200 East Ninth Ave., Denver 20, Colo. Annual meeting to be announced.

San Antonio-Military Radiological Society
Secretary, Dr. Hugh F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Tex. Meets third Wednesday each month in Fort Sam Houston Officer's Club at 6:30 P.M.

San Diego Radiological Society
Secretary, Dr. Charles G. Campbell, 6673 Avenida Manana, La Jolla, Calif. Meets first Wednesday of each month at the University Club.

San Francisco Radiological Society
Secretary, Dr. Walter Coulson, San Francisco General Hospital, San Francisco 8, Calif. Meets quarterly at the San Francisco Medical Society, 250 Masonic Ave., San Francisco 18, Calif.

Section on Radiology, California Medical Association
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary-Treasurer, Dr. Martin A. Thomas, 1150 Connecticut Ave., Washington 6, D. C. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Southern Medical Association
Secretary, Dr. John D. Reeves, Department of Radiology, Univ. of Florida College of Medicine, Gainesville, Fla. Annual Meeting: New Orleans, La., Nov. 18–21, 1963.

Section on Radiology, Texas Medical Association
Secretary, Dr. George F. Crawford, St. Elizabeth Hospi-

tal, Beaumont, Tex. Meets annually with the Texas Medical Association.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

SOCIETY FOR PEDIATRIC RADIOLOGY
Secretary, Dr. John L. Gwinn, Children's Hospital, Los Angeles 27, Calif. Annual meeting: Queen Elizabeth Hotel, Montreal, Que., Canada, Oct 7, 1963.

SOCIETY OF NUCLEAR MEDICINE
Secretary, Mr. C. Craig Harris, Oak Ridge National Laboratories, Oak Ridge, Tenn. *Administrator*, Mr. Samuel N. Turiel, 430 N. Michigan Ave., Chicago 11, Ill. Annual meeting to be announced.

SOUTH BAY RADIOLOGICAL SOCIETY
Secretary, Northern Section: Dr. John S. Wilson, 1515 Trousdale Dr., Burlingame, Calif.; Southern Section: Dr. A. C. Mitchell, 728 Cass, Monterey, Calif. Meets second Wednesday of each month.

SOUTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

SOUTHERN RADIOLOGICAL CONFERENCE
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 4097, Mobile, Ala. Annual meeting: Grand Hotel, Point Clear, Ala., Jan. 31–Feb. 2, 1964.

SOUTHWESTERN RADIOLOGICAL SOCIETY
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. B. M. Brady, St. Joseph Hospital, Memphis, Tenn. Meets annually at the time and place of the Tennessee State Medical Association meeting.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon, 402 Professional Bldg., 1216 Pennsylvania Ave., Fort Worth 4, Tex. Annual meeting: Dallas, Tex., Jan. 31–Feb. 1, 1964.

TRI-STATE RADIOLOGICAL SOCIETY
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital, Ann Arbor, Mich.

UPPER PENINSULA RADIOLOGICAL SOCIETY
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

UTAH STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Richard Y. Card, St. Mark's Hospital, Salt Lake City, Utah. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

VERMONT RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Williams, 160 Allen St., Rutland, Vt.

VIRGINIA RADIOLOGICAL SOCIETY
Secretary, Dr. Powell G. Dillard, Jr., 715 Church Street, Lynchburg, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Robert H. Rosenberg, 7011 38th Ave., N.E., Seattle 15, Wash. Meets quarterly.

WEST VIRGINIA RADIOLOGICAL SOCIETY
Secretary, Dr. Karl J. Myers, The Myers Clinic-Broaddus Hospital, Philippi, W. Va. Meets concurrently with Annual Meeting of West Virginia State Medical Society; other meetings arranged by program committee.

WESTCHESTER RADIOLOGICAL SOCIETY
Secretary, Dr. Edward T. Bello, Westchester Academy of Medicine, Section on Radiology, Purchase, N. Y. Meets on third Tuesday of January and October and on two other dates.

WISCONSIN RADIOLOGICAL SOCIETY
Secretary, Dr. Charles Benkendorf, 408 St. Francis St., Green Bay, Wis. Annual meeting each spring in various places.

CUBA, MEXICO, PUERTO RICO AND CENTRAL AMERICA

ASOCIACIÓN DE RADIÓLOGOS DE CENTRO AMERICA Y PANAMÁ. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá.
Secretary-General, Dr. Raul Arguello, 5a. Ave., Norte No. 48, San Salvador, El Salvador. Meets annually in a rotating manner in the six countries.

SOCIEDAD DE RADIOLOGÍA DE EL SALVADOR
Secretary, Dr. Rafael Vaga Gómez.

SOCIEDAD DE RADIOLOGÍA DE GUATEMALA
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPÍA CUBANA
Secretary, Dr. Miguel A. García Plasencia, Hospital Curie, 29 y F, Vedado, Habana, Cuba. Meets monthly at Curie Hospital.

SOCIEDAD COSTARRICENSE DE RADIOLOGIA
Secretary, Dr. James Fernández Carballo, Apartado VIII, San José, Costa Rica.

SOCIEDAD MEXICANA DE RADIOLOGÍA, A. C.
Calle del Oro No. 15, México 7, D. F.
Secretary-General, Dr. E. Alvarez Hernández.
Meets first Monday of each month.

ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

SOCIEDAD RADIOLÓGICA PANAMEÑA
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

SOCIEDAD RADIOLÓGICA DE PUERTO RICO
Secretary, Dr. Jorge Carreras Girard, Suite 504, Professional Bldg., Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

BRITISH COMMONWEALTH OF NATIONS

ASSOCIATION OF RADIOLOGISTS OF THE PROVINCE OF QUEBEC
Secretary, Dr. R. Robillard, Notre-Dame Hospital, 1560 Sherbrooke St., East, Montreal, Que., Canada. Meets four times a year.

BRITISH INSTITUTE OF RADIOLOGY
Honorary Secretary, Dr. R. D. Hoare, 32 Welbeck St., London, W. 1, England. Meets monthly from October until May.

CANADIAN ASSOCIATION OF PHYSICISTS, DIVISION OF MEDICAL AND BIOLOGICAL PHYSICS.
Honorary Secretary-Treasurer, Paul M. Pfalzner, Dept. of Therapeutic Radiology, University of Western Ontario, London, Ont., Canada. Annual meeting: Halifax, Nova Scotia, June, 1964.

EDMONTON AND DISTRICT RADIOLOGICAL SOCIETY
Secretary, Dr. J. T. Mason, 540 Tegler Bldg., Edmonton, Alberta, Canada. Meets second Tuesday of each month, October to May.

FACULTY OF RADIOLOGISTS
Honorary Secretary, Dr. C. J. Hodson, 47 Lincoln's Inn Fields, London, W.C.2, England. Annual meeting to be announced.

FACULTY OF RADIOLOGISTS, ROYAL COLLEGE OF SURGEONS IN IRELAND
Registrar, Dr. H. O'Flanagan, F.R.C.P.I., D.P.H., 123 St. Stephens Green, Dublin 2, Ireland.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1, England.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. D. J. Sieniewicz, *Associate Honorary Secretary-Treasurer*, Dr. Maurice Dufresne 1555 Summerhill Ave., Montreal 25, Que., Canada. Annual meeting: Hotel Vancouver, Vancouver, B.C., Feb. 29–March 4, 1964.

Montreal Radiological Study Club
Secretary, Dr. Leonard Rosenthall, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electro-Radiologie Médicale
General Secretary, Dr. Maurice Dufresne, 1560 Sherbrooke (East), Montreal, Que., Canada. Meets third Saturday each month.

Toronto Radiological Society
Secretary, Dr. Wallace M. Roy, St. Joseph's Hospitals, 30 The Queensway, Toronto 3, Ont., Canada. Meets second Monday of each month September through May.

College of Radiologists of Australia
Honorary Secretary, Dr. E. A. Booth, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

South America

Asociación Argentina de Radiología
Secretary, Dr. Lidio G. Mosca, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Ateneo de Radiologia
Secretary, Dr. Victor A. Añaños, Instituto de Radiologia, Santa Fe 3100, Rosario, Argentina. Meets monthly on second and fourth Fridays at 7:00 P.M. in the Hospital Nacional del Centenario, Santa Fe 1300, Rosario.

Colégio Brasileiro de Radiologia
Secretary-General, Dr. Tede Eston de Eston, Caixa Postal 5984, São Paulo, Brazil.

Sociedad Argentina de Radiologia
Secretary, Dr. Armando B. de Onaindia, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Bolivana de Radiología
Secretary, Dr. Javier Prada Méndez, Casilla 1596, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Nicola Caminha, Av. Mem. de Sa, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. J. P. Velasco, Avenida Santa María 0410, Santiago, Chile. Meets fourth Friday of each month.

Sociedad Colombiana de Radiologia
Secretary, Dr. Alberto Mejía Diazgranados, Carrera 13, No. 25–31, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología y Fisioterapía
Secretary, Dr. Luis Blum, P.O. Box 3712, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary, Dr. Vicente Ubillus, Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta 218, Lima.

Sociedad de Radiologia del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41–110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiologia.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. Ernesto H. Cibils, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiologia de Pernambuco
Secretary, Dr. Manoel Medeiros, Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad de Roentgenologia y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Carlos A. Oulton, Santa Rosa 447, Córdoba, Argentina.

Sociedad Venezolana de Radiología
Secretary-General, Dr. Rubén Merenfeld, Apartado No. 9362, Candelaria, Caracas, Venezuela. Meets monthly third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik.

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 256 Chaussée de Wavre, Heverlee-lez-Louvain, Belgium. Meets in February, March, May, June, October, November and December.

Société Française d'Electroradiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
Secretary-General, Dr. Ch. Proux, 9 rue Daru, Paris 8ᵉ, France.

Československá Společnost pro Roentgenologii a Radiologii
Secretary, Dr. Robert Poch, Praha 12, Šrobárova 50, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Deutsche Röntgengesellschaft
Secretary, Professor Dr. med. H. Lossen, Universitäts-Röntgeninstitut., Lagenbeckstr. 1, Mainz, Germany.

Società Italiana di Radiologia Medica e di Medicina Nucleare
Secretary, Dr. Ettore Conte, Ospedale Mauriziano, Torino, Italy. Meets annually.

Nederlandse Vereniging voor Radiologie
Secretary, Dr. H. F. O. Stricker, Schalklaar, Netherlands.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Española de Radiología y Electrología Médicas y Medicina Nuclear
Secretary, Dr. D. Aureo Gutierrez Churruca, Esparteros, No. 9, Madrid, Spain. Meets monthly in Madrid.

Schweizerische Gesellschaft für Radiologie und Nuklearmedizin (Société Suisse de Radiologie et de Médecine Nucléaire)
Secretary. Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

Asia

Indian Radiological Association
Secretary Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

Indonesian Radiological Society
Secretary Professor Sjahriar Rasad Taman Tjut Mutiah 1, Diakarta, Indonesia.

ABSTRACTS OF RADIOLOGICAL LITERATURE

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Head

Soyka, D.: Basilar impression; a contribution to neuroradiologic diagnosis and clinical symptomatology........ 1101
Lorber, J., and Grainger, R. G.: Cerebral cavities following ventricular punctures in infants........ 1101

Neck and Chest

Bock, K. *et al.*: Aplasia of a pulmonary artery. 1101
Platten, P. M., and Parks, R. E.: Radiographic diagnosis of thymic tumors........ 1101
Rayl, D. F., and Spjut, H. J.: Bronchographic crystalline-inclusion pneumonia due to hytrast........ 1101

Abdomen

Juhl, J. H., Cooperman, L. R., and Crummy, A. B.: Oragrafin, a new cholecystographic medium; a double-blind comparison with telepaque........ 1102

Gynecology and Obstetrics

Weinberg, C. R., Ciccalese, G., and Abbasoglu, S.: Radiological diagnosis of extra-uterine pregnancy........ 1103
Swartz, D. P., Platt, M. A., and Heagy, F. C.: Radioisotope (I^{131}) studies of placental location and circulation........ 1103
Van Ostrand, J. R., Wellenbach, B., and Fineberg, C.: Vascular lesions of the female pelvis: with report of an aneurysm with arteriovenous fistula of the uterine artery and vaginal vein........ 1103
Kittredge, R. D. *et al.*: An illustration of an approach to the diagnosis of pelvic disease........ 1104

Genitourinary System

Opit, L. J., Proudman, W. D., and Bonnin, N. J.: Renal papillary necrosis........ 1104
Adeney, N. F., and Fraser, G. A.: Renal angiography by retrograde femoral catheterization as an aid to diagnosis of renal tumors........ 1105
Uson, A. C., Melicow, M. M., and Lattimer, J. K.: Is renal arteriography (aortography) a reliable test in the differential diagnosis between kidney cysts and neoplasms?...... 1105
Lang, E. K. *et al.*: Retrograde arteriography in the diagnosis of bladder tumors........ 1105
Abrams, H. L., Boijsen, E., and Borgström, K.-E.: Effect of epinephrine on the renal circulation; angiographic observations........ 1106
Kaufman, J. J., Schanche, A. F., and Maxwell, M. H.: Excretory urography in the diagnosis of renovascular hypertension; methods of enhancing its value........ 1106
Doig, A. *et al.*: ^{131}I-"Hippuran" renography in detection of unilateral renal disease in patients with hypertension........ 1107
Lawrence, J. R. *et al.*: Value of ^{131}I-"Hippuran" renography in urological investigation........ 1107
Van Velzer, D. A., Burge, C. H., and MacIntyre, R. S.: Clinical evaluation of a new medium for excretory urography: a comparison study of renovist and renografin 76 per cent........ 1107
MacEwan, D. W.: Demonstration of ureteral stump reflux by voiding cystourethrography during excretory pyelography........ 1108

Skeletal System

Bywaters, T. W., Jr. *et al.*: Infantile cortical hyperostosis presenting with exophthalmos: case report........ 1108
Scott, T. F., and Bailey, R. W.: Idiopathic scoliosis in fraternal twins........ 1108
Epstein, J. A., Epstein, B. S., and Lavine, L. S.: Cervical spondylotic myelopathy.... 1109
Vallebona, D.: Osteophytosis and syndesmophytosis........ 1109
Wells, L. H.: Congenital deficiency of the vertebral pedicle........ 1109
Mead, C. A., and Martin, M.: Aplasia of the trochlea—an original mutation........ 1109
Paus, B. C., and Kim, T. K.: Osteoid osteoma of the spine........ 1110
Friedenberg, Z. B.: Protrusio acetabuli in childhood........ 1110
Wray, J. B., and Herndon, C. N.: Hereditary transmission of congenital coalition of the calcaneus to the navicular........ 1110
Stein, A. H., Jr.: The relation of median nerve compression to Sudeck's syndrome........ 1110
Jeffreys, T. E.: The painful heel in adolescence........ 1111
Denham, R. H., Jr., and Dingley, A. F., Jr.: Fibrosarcoma occurring in a draining sinus. 1111

Dragoni, G., and Salvini, E.: Clinical and radiologic study of plasmocytoma: (considerations of 43 cases) 1111
Bose, K. S., and Chowdhuri, B.: Observations on synovial sarcoma 1111
Vose, G. P.: Fine structure of bone as seen on fracture and cleavage planes by electron microscopy 1112

Blood and Lymph System

Goffrini, P.: Radiopaque injection of the thoracic duct: morphologic and functional observations on lymphatic circulation when the subphrenic and mediastinal lymph nodes are blocked by neoplastic involvement 1112
Pelkey, W. J., Powell, P. R., and Fagan, W. T.: Experiences with lymphangiography 1113
Wohlgemuth, J.: A simple injector for lymphangiography 1113
Bron, K. M., Baum, S., and Abrams, H. L.: Oil embolism in lymphangiography: incidence, manifestations, and mechanism 1113

General

Hall, P.: Albright's syndrome in an adult male: report of an atypical case with psychiatric symptoms 1114
Montgomery, M. M. *et al.:* Reiter's syndrome 1114
Pace, W. R., Jr., Decker, J. L., and Martin, C. J.: Polymyositis: report of two cases with pulmonary function studies suggestive of progressive systemic sclerosis 1114
Slim, M. S., and Sieber, W. K.: Unusual manifestations of staphylococcic infection in infants and children 1114
Johnston, R. F., Green, R. A., and Headington, J. T.: Progressive multifocal leukoencephalopathy 1115
Watson, J. C., Weinstein, A. S., and Greenspan, R. H.: Advantages of three-phase spot-film radiography 1115

RADIATION THERAPY

Watson, T. A., and Campbell, J. M.: Supervoltage radiation therapy in advanced cancer of the urinary bladder 1115
Jacobs, L. G.: Unusual case of late postirradiation damage to the ileum 1116

RADIOISOTOPES

Skillern, P. G., McCullagh, E. P., and Clamen, M.: Radioiodine in diagnosis and therapy of hyperthyroidism 1116
Kusakabe, T., and Miyake, T.: Defective deiodination of I^{131}-labeled L-diiodotyrosine in patients with simple goiter 1117
Gabriel, J. B. *et al.:* Evaluation of chromic oxide marker in absorption of fat 1117
Malinow, M. R. *et al.:* Vascular and extravascular radioactivity after the injection of estradiol 6,7H^3 in the human being 1118
Chang, M. C., Hunt, D. M., and Harvey, E. B.: Effects of radiocobalt irradiation of pregnant rabbits on the development of fetuses 1118
Dixon, A. D., and Hoyte, D. A. N.: A comparison of autoradiographic and alizarin techniques in the study of bone growth 1118

ROENTGEN DIAGNOSIS

Head

Soyka, D. Basiläre Impression; (ein Beitrag zur neuroradiologischen Diagnostik und klinischen Symptomatologie). (Basilar impression; [a contribution to neuroradiologic diagnosis and clinical symptomatology].) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, April, 1963, *98*, 483–488. (Address: Universitäts-Nervenklinik mit Poliklinik, Erlangen, Germany.)

Twelve cases with basilar impression of the skull are described by the author. Not only the roentgenologic diagnosis is considered, but also the clinical symptomatology.

The roentgen findings are those of elevation of the dens and an abnormal shape of the occipital bone. Six different linear and angular measurements were available for study of this anomaly or disease. Neurologically there may be 8th nerve findings or nystagmus or cerebellar ataxia. Occasionally, a hydrocephalus may be present. Many patients with these findings show no evidence of symptoms.—*Hans W. Hefke, M.D.*

Lorber, John, and Grainger, Ronald G. Cerebral cavities following ventricular punctures in infants. *Clin. Radiol.*, April, 1963, *14*, 98–109. (From: Department of Child Health, The University of Sheffield and the Department of Radiology, The Children's Hospital, Sheffield, England.)

It is widely recognized that air may be seen in the needle track at the time of ventriculography. It is generally assumed that this air is soon absorbed without permanent cerebral damage. The authors show that such tracks may develop into large cerebral cavities.

To date, it has not been possible to attribute clinical signs and symptoms to the development of these intracerebral cavities, possibly because they occur in a relatively silent area of the brain, in the frontal lobes.

The air-filled tracks or cavities may only be seen on roentgenograms made in the erect or brow-up position, and anteroposterior and lateral views should always be obtained in these positions. When multiple ventricular punctures are necessary for the treatment of meningitis, the resulting cerebral cavities are larger and multilobular. Because of insufficient cerebral tissue to accommodate a cavity, none of 80 infants with extreme hydrocephalus developed demonstrable cavities even after multiple punctures. In neurologically handicapped patients, no additional clinical impairment could be attributed to these post-traumatic cavities.—*Samuel G. Henderson, M.D.*

Neck and Chest

Bock, K., Richter, H., Trenckmann, H., and Herbst, M. Die Aplasie einer Lungenarterie. (Aplasia of a pulmonary artery.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, April, 1963, *98*, 419–427. (Address: Dr. K. Bock, Univ.-Kinderklinik, Leipzig, Germany.)

An isolated aplasia of a pulmonary artery is a rare anomaly. More often it is seen in agenesis of the lung or cardiac anomalies. Until 1958 only 11 cases had been described in the literature.

In the authors' patients, the left pulmonary artery was absent. The anomaly is of symptomatic significance. The cases were noted in patients with lung agenesis and congenital heart disease.

Six additional cases are described with roentgenographic and angiographic reproductions.—*Hans W. Hefke, M.D.*

Platten, Philip M., and Parks, Raymond E. Radiographic diagnosis of thymic tumors. *South M. J.*, Aug., 1963, *56*, 817–823. (From: Departments of Radiology, University of Miami School of Medicine, and Jackson Memorial Hospital, Miami, Fla.)

The authors report their experience with the roentgenographic appearance of 21 cases of thymic tumor. Ten were associated with myasthenia gravis, 2 with anemia. Other conditions reported to occur with thymomas, but not seen in this series, were pancytopenia, agammaglobulinemia and Cushing's syndrome. The symptoms of dyspnea and pressure correlated well with the tumor size.

Location was of little diagnostic aid as thymic tumors may occur any place between the neck and diaphragm. Smaller tumors often are adjacent to the aortic arch and may show linear calcifications. Differentiation from an aortic aneurysm is difficult as aortic pulsations are usually transmitted to the tumor. Larger tumors tend to extend inferiorly and lie in the anterior and/or middle mediastinum, simulating lymphoma. Laminagraphy in a slightly oblique position is of aid in recognition and localization of calcification. Mottled calcifications are reported to indicate malignancy but this type was not found in the authors' series. Contrast vascular studies, particularly venous angiography, help to show the extent of the tumor. Pneumomediastinum was unsuccessful in the one attempt made.—*Barry Gerald, M.D.*

Rayl, Donald F., and Spjut, Harlan J. Bronchographic crystalline-inclusion pneumonia due to hytrast. *Radiology*, April, 1963, *80*, 588–604. (Address: 510 South Kingshighway, St. Louis 10, Mo.)

Hytrast is a new aqueous bronchographic contrast medium which has been found to have many excellent properties. As with other aqueous contrast agents, however, it is somewhat irritating to the bronchial mucosa. This factor plus the property of having greater mucosal adhesiveness probably accounts for the more severe postbronchographic reactions than are seen when the oily bronchographic media are used. The authors feel that the irritating effect excites a protective response in the lung of cough, ciliary action, mucus production and exudation. These effects enable the hytrast to penetrate further than at the initial point at the time of bronchography, resulting in peripheral dissemination and "alveolar filling." Since the distal bronchial tree lacks the protection of ciliary expulsive action and mucus covering the mucosa and the agent comes into direct contact with this mucosa, an inflammatory reaction occurs resulting in pneumonia.

Studies on the lungs of a series of dogs on whom bronchography was performed using hytrast and other contrast media showed that the inflammatory reaction and pneumonia seen after using hytrast was secondary to the presence of hytrast crystals in the bronchi and alveoli. This crystalline-inclusion pneumonia was acute, even with areas of necrosis. Cultures of the hytrast used showed that this was a chemical pneumonia and not due to bacteria introduced in the medium.

In the authors' series of 18 patients who had bronchographic examinations using hytrast as the contrast medium, 2 had the significant complication of pneumonia. These patients were clinically ill with dyspnea and fever in addition to the roentgenographic picture of pneumonia. A review of the other cases showed temperature elevation as well as small areas of pneumonia on the roentgenograms more often than not. The studies on the lungs of the dogs showed that similar but less acute changes occurred also with the oily media but that recovery was slower. While this acute crystalline-inclusion pneumonia was found more often than not in man, complete recovery occurred in all instances with no evidence of permanent roentgen changes. Complete resolution of the minor changes was usually observed in 5 to 7 days, and in the severe reactions in about 2 weeks.

The authors conclude that the direction of future investigation for an ideal contrast medium for bronchography should be toward an aqueous agent with the excellent contrast of hytrast but without its irritating and inflammation-inciting properties.

Many excellent reproductions of the roentgenograms and the photomicrographs of the pulmonary changes in man and dogs, demonstrating the character of bronchographic crystalline-inclusion pneumonia, are presented.—*Donald N. Dysart, M.D.*

ABDOMEN

Juhl, J. H., Cooperman, L. R., and Crummy, A. B. Oragrafin, a new cholecystographic medium: a double-blind comparison with telepaque. *Radiology*, Jan., 1963, *80*, 87–91. (From: Department of Radiology, University of Wisconsin Medical School, Madison, Wis.)

The authors report on their study of a new cholecystographic medium, oragrafin. Chemically it is the sodium salt of B-3-dimethylaminomethylenemino-2,4,6-triiodophenyl-propionic acid. It has an iodine content of 61.4 per cent and is available in granules put up in capsules and in a water-soluble form as a calcium salt. Reports in the European literature have indicated that oragrafin is excreted by the liver in sufficient quantity to opacify the extrahepatic biliary ducts without concentration by the gallbladder. In these reports a second dose of medium was given the morning of the roentgen examination in addition to the usual evening dose.

In this study the authors compared the value of this medium in cholecystography with telepaque, a medium with which they have had considerable experience. Their usual standard cholecystographic procedure was followed in all of the 200 patients covered in this double-blind study. One hundred patients received telepaque and 100 received oragrafin. All patients were interviewed by one of the authors and the roentgenograms interpreted without knowledge of which particular medium was involved. The side reactions in all instances were minimal to moderate. Nine of the oragrafin and 11 of the telepaque group experienced nausea. Vomiting occurred in 2 subjects in each group. Only 3 patients in the oragrafin group had diarrhea as compared to 14 in the telepaque group, and only 1 patient in the oragrafin group had a loose stool as compared to 15 of those receiving telepaque.

Very little difference was noted in the gallbladder visualization in the two groups. Eighty-four of the oragrafin patients had enough opacification for diagnosis, as compared to 88 of the telepaque group. Nonvisualization was more frequent with oragrafin—11 cases compared to 6 with telepaque. In none of the patients was the visualization of the common bile duct comparable to that obtained in a good quality intravenous cholangiogram. Twelve of the oragrafin and 10 of the telepaque group showed opacification of the duct sufficient to outline most of its length and to measure its caliber. Faint visualization was present more often with telepaque than with oragrafin but was insufficient for diagnosis. Forty-nine telepaque patients and 15 oragrafin patients had a residue within the gastrointestinal tract but for the most part none of this residue interfered with diagnostic accuracy. Cholelithiasis was present with almost identical incidence in both groups of patients. The cases of nonvisualization of the gallbladder were investigated and although there were almost twice as many of these among the oragrafin patients than among the telepaque patients it was felt that the difference in number was primarily a result of the chance examination of more pathologic gallbladders in the oragrafin group.

Since no attempt was made to outline the biliary duct system by altering the routine cholecystographic procedure employed in the authors' department no opinion is given regarding the value of either medium for visualization of the bile ducts. It is felt, however, that oragrafin is equal to telepaque as a gallbladder-opacifying medium and is preferable to it in respect to side-effects and gastrointestinal residues.—*Donald N. Dysart, M.D.*

Gynecology and Obstetrics

Weinberg, C. Richard, Ciccalese, Gerald, and Abbasoglu, Semir. Radiological diagnosis of extra-uterine pregnancy. *Radiology*, Jan., 1963, *80*, 69–75. (From: Department of Radiology, Martland Medical Center, Newark City Hospital, Newark, N. J.)

The authors have compiled 8 roentgen criteria which they consider pathognomonic for the diagnosis of extra-uterine pregnancy. The criteria are listed in the order in which they were most frequently seen.

1. Abnormal position and presentation of the fetus: Usually eccentric: "transverse lie" or breech presentation; presenting part not "engaged" (unless vertex or feet are in the cul de sac).
2. Absence of the gravid uterine and placental shadows in their "normal" position; a thin amniotic sac must not be mistaken for the uterus.
3. Unusual sharpness and clarity of the fetus and fetal parts.
4. Intermingling of the maternal gaseous shadows with the fetal parts.
5. Unchanging position of the fetus on serial studies; the fetus will always remain in the position noted on the first study.
6. Presence of a pelvic or lower abdominal mass, which may be the slightly enlarged uterus or placenta. Hysterogram may be done for confirmation if the mass is suspected to be the uterus either on the roentgenogram or by manual examination.
7. Close proximity of the fetus to the maternal abdominal wall, seen on the lateral roentgenogram when the fetus is in the transverse position.
8. Fetal parts overlying the maternal spine, seen on the lateral roentgenogram, which must be "true," most often when the fetus is in the transverse position.

The first criterion was observed in almost every case of extra-uterine pregnancy, but the second of the criteria is considered the most reliable of all.

It is advised that in all cases where abnormal position and presentation are clinically suspected, anteroposterior and lateral roentgenograms be made of the abdomen, preferably in the last trimester of pregnancy. Hysterography may be necessary to establish the diagnosis. Fetal mortality and maternal morbidity can be reduced if the radiologists recognize the fact that this entity can be diagnosed with greater accuracy by the routine anteroposterior and lateral roentgenograms than by clinical evaluation.—*A. W. Sommer, M.D.*

Swartz, Donald P., Platt, Melville A., and Heagy, Fred C. Radioisotope (I^{131}) studies of placental location and circulation. *Am. J. Obst. & Gynec.*, Feb., 1963, *85*, 338–344. (From: Departments of Obstetrics and Gynaecology, Therapeutic Radiology, University of Western Ontario, and Ontario Cancer Foundation, London Clinic, London, Ontario, Canada.)

Placental localization using radioactive tracers has been described by a number of groups in the past but has never achieved general acceptance. The authors describe their results in a series of 66 patients in whom the following method was employed: a dose of 3 μc of radioactive iodinated human serum albumin containing I^{131} was injected into an antecubital vein. After 10 minutes a collimated scintillation detector connected to a count rate meter was used to count radioactivity in a reference position over the heart blood pool and in 21 positions on the anterior body wall to map the position of the placenta within the uterus. Large doses of iodide were administered before undertaking the procedure in order to block maternal and fetal thyroid glands. Lateral and posterior readings were occasionally found to be of value.

The authors are satisfied that this test yields a high percentage of accuracy in placental localization and believe it to be of value in the differential diagnosis of antepartum hemorrhage. By incidental study of a group of mothers in whom fetal death had occurred, evidence was adduced to suggest that there may be differences in the maternal placental circulation which vary with the duration of retention of a dead fetus. There may be an early period of marked reduction of maternal placental blood flow, followed by a later return to a normal, or even high, level.—*Frederick J. Bonte, M.D.*

Van Ostrand, J. R., Wellenbach, B., and Fineberg, C. Vascular lesions of the female pelvis: with report of an aneurysm with arteriovenous fistula of the uterine artery and vaginal vein. *Am. J. Obst. & Gynec.*, April, 1963, *85*, 966–969. (From: Jefferson Hospital, Philadelphia 7, Pa.)

Rarity of vascular lesions in the female pelvis is emphasized by reviewing the literature on the subject. Aneurysm of the iliac artery in the female is apparently quite rare, but arteriovenous fistula involving uterine blood vessels may be more common as indicated by Borell's work including pelvic arteriography on over 500 women.

The authors present a case report in which a large asymptomatic pulsating mass was along the left lateral vaginal wall. The nature of the lesion was determined by needle aspiration and retrograde femoral arteriography. Following successful surgical removal the patient underwent postoperative arteriography which indicated complete cure. The aneurysm in this case was of uterine artery origin and the fistula joined with the vaginal vein. The etiology in this, as in most other cases, remains speculative.—*Richard E. Kinzer, M.D.*

Kittredge, Richard D., Burger, Robert, Finby, Nathaniel, and Draper, John W. An illustration of an approach to the diagnosis of pelvic disease. *J. Urol.*, April, 1963, *89*, 607–610. (From: Departments of Radiology and Urology, St. Luke's Hospital, New York, N. Y.)

This article includes a brief summary of the various methods now available for the study of certain forms of pelvic disease. In carefully selected patients who present diagnostic problems, a combination of arteriography, venography, and lymphangiography may be a valuable supplement to the customary roentgen diagnostic procedures. Arteriography in this location may differentiate benign from malignant mass lesions and the relation of such lesions to adjacent organs. It is also of value in noting the degree of vascularization present in any tumefaction.

Venography in the study of pelvic disease has been valuable in the localization of metastatic tumors and the diagnosis of thrombus or tumor in the renal vein, vena cava, or great pelvic veins. Lymphangiography will show blocked lymphatics, involved lymph nodes, and displacement of vessels and lymph nodes. All of these methods have been successfully used in one patient whose record is summarized in this article. This patient presented a problem of differential diagnosis between recurrent cancer from primary carcinoma of the cervix and postirradiation fibrosis. The combined roentgenographic studies did not confirm neoplastic recurrence and suggested a benign process probably radiation fibrosis.

Four figures are used to illustrate the findings.—*George W. Chamberlin, M.D.*

GENITOURINARY SYSTEM

Opit, L. J., Proudman, W. D., and Bonnin, N. J. Renal papillary necrosis. *Brit. J. Surg.*, Jan., 1963, *50*, 375–381. (From: The University Department of Surgery, Queen Elizabeth Hospital, Woodville, South Australia.)

Prior to 1954 only 6 cases had been reported in which this diagnosis was correctly made ante mortem.

Papillary necrosis remains a vague entity. Of particular importance is whether the pathologic lesion of papillary necrosis is part of a single disease entity, or is the result of many different processes, perhaps having a common anatomic and pathologic abnormality as their end-result.

Ten cases are summarized in detail. Cases 1–8 are presented as cases of severe loin pain or ureteric colic with pyuria. This was almost certainly due to the passage or impaction of necrotic papillary fragments. All these patients were women. They have been labelled Group 1.

In Cases 9 and 10 the papillary necrosis was discovered incidentally at autopsy, both patients having had severe pyelonephritis.

Every case showed pyuria with a familiar distribution of organisms, a positive culture of *E. coli* being present in 4 cases and *P. vulgaris* in 5 cases. Six cases had anemia, usually normocytic.

A significant and surprising fact was the degree of medullary destruction and pelvic obstruction associated with normal blood urea nitrogen.

Plain roentgenography may show enlargement of the kidney with sufficient perirenal edema to obscure the psoas shadow. Further clues may be the presence of faint calcific shadows, triangular or quadrangular in shape, seen within the renal areas. The preeminent diagnostic criteria are the characteristic pyelographic changes. Every case in Group 1 exhibited these, as a non-filling of a calyceal group. Later a cavity at this site with excavation of the medulla occurs, or a small medullary cavity with the characteristic triangular nonopaque filling defect within it can be seen. Also extensive bilateral lesions with gross excavation and irregular cavities in the medullary substance can be found. Minor calyceal cavitation coinciding with acute attacks of loin pain can be regarded as a highly suspicious sign.

The necrotic fragments are passed, producing ureteric colic or fixed loin pain. The diagnostic features of the pyelogram owe their characteristic appearances to the separation of these fragments.

It is likely that endarteritis coupled with sufficient obstruction from inflammatory edema could lead quite nonspecifically to papillary necrosis, especially if pyramidal blood supply is vulnerable.

A common association between papillary necrosis and heavy phenacetin-taking is also confirmed.

A second pathologic process supervenes in a number of cases and this produces the presentation characterized by the Group 1 cases. This process begins with pelvic or ureteric obstruction, with subsequent occurrence, or aggravation, of severe urinary infection. This infection itself produces further medullary destruction. If unrelieved a vicious cycle of obstruction and infection is initiated.

Most authors counsel against resection of the kidney unless it has been completely destroyed. Where the obstructive symptoms dominate the clinical picture, retrograde catheterization, ureteric lavage and suction drainage, utilizing, if necessary, two or three catheters in a single ureter, are important factors in relieving the obstruction and overcoming the infection.

Where dense calcification of papillary fragments has occurred or where lavage is ineffective, pyelotomy may be required; it is necessary to continue systemic antibiotics after this. Also, one may consider the rational use of steroids, although where severe and fulminating infections are likely the dangers of steroid therapy must be fully appreciated.—*Stephen N. Tager, M.D.*

Adeney, N. F., and Fraser, G. A. Renal angiography by retrograde femoral catheterization as an aid to diagnosis of renal tumors. *Brit. J. Surg.*, Jan., 1963, *50*, 427–431. (From: Poole General Hospital, England.)

The authors point out that in the majority of cases of renal tumors the standard methods of investigation with intravenous and retrograde pyelography, in conjunction with clinical findings, give sufficient evidence for exploration. Occasionally, when the tumor is small, and situated at the upper pole of the kidney, the intravenous and retrograde pyelograms may be inconclusive. Two such cases are reported, with follow-up studies by renal angiography.

Renal angiographic studies were made by percutaneous retrograde catheterization of the femoral artery. These showed the characteristic irregular "tufted" tumor vessels, and puddling of the contrast medium in parts of the tumor area indicating increased vascularity.

The authors have used this technique in renal angiographic studies of 103 patients in the past 4 years; they discuss the possible advantages over the translumbar aortography.

Case reports and reproductions of roentgenograms are included.—*Douglas S. Kellogg, M.D.*

Uson, Aurelio C., Melicow, Meyer, M., and Lattimer, John K. Is renal arteriography (aortography) a reliable test in the differential diagnosis between kidney cysts and neoplasms? *J. Urol.*, April, 1963, *89*, 554–559. (From: Squier Urological Clinic, Columbia-Presbyterian Medical Center, New York, N. Y.)

This excellent article calls our attention to the diagnostic pitfalls which unless recognized may lead to erroneous conclusions in a serious disease of the kidney. In a review of 70 aortograms, the authors found 5 instances in which the diagnosis of renal cyst was made in patients who subsequently were shown to have malignant lesions of the kidney. These 5 cases are reported in detail. The lesions encountered in these 5 diagnostic errors were (1) renal cell carcinoma with necrosis, (2) solid tubular adenoma, (3) papillary cystadenocarcinoma, (4) renal carcinoma with metastasis, and (5) papillary cystadenoma. In all these instances, the renal arteriogram was interpreted as negative for neoplasm on the basis of absence of pooling and lack of increased blood supply to the involved kidney.

These roentgenographic signs, in the presence of an expanding mass, are considered to be pathognomonic for renal carcinoma, but the absence of these findings does not indicate that the lesion is a benign cyst. Some types of renal tumors, such as cystadenomas, as well as certain renal and capsular neoplasms, may show relatively avascular structure on the arteriogram. For these reasons, it is important to rely upon positive findings as shown by pyelography and to use surgical exploration in those instances where the diagnostic features of arteriography are not clearly those of a neoplasm or of a benign cystic process.—*George W. Chamberlin, M.D.*

Lang, Erich K., Wishard, W. Niles, Jr., Nourse, Myron H., and Mertz, J. H. O. Retrograde arteriography in the diagnosis of bladder tumors. *J. Urol.*, Mar., 1963, *89*, 422–426. (From: Department of Radiology, Methodist Hospital, Indianapolis, Ind.)

It is now generally recognized that the prognosis of patients with bladder carcinoma is dependent upon the depth of infiltration and penetration of the tumor into the muscular wall or perivesical fat. The clinical evaluation and the therapeutic approach to these tumors have been enhanced by the use of retrograde arteriography.

The authors employ the technique of Seldinger. The femoral artery is entered into percutaneously and a catheter passed either to the level of the lower aorta just above the bifurcation or directly into the hypogastric artery for selective arteriography. For selective angiography 10 cc. of 50 per cent contrast medium is used, but for the "flushing technique" 30 cc. of 90 per cent contrast medium is preferred. Serial exposures are made over a period of 8 seconds following injection. In certain patients a second injection is carried out to show the tumor in a tangential position in relation to the bladder wall. The lumen of the bladder may be contrasted by the introduction of carbon dioxide or nitrous oxide through a Foley catheter.

This method of examination has proved to be particularly valuable in the differentiation of lesions of Stage B_2 and C. The advantage of arteriography lies in the selective visualization of the tumor for therapeutic purposes. The positive stain of the tumor, the cork-screw vessels, and the large vessels of the base of the tumor allow accurate staging and localization. The benign tumors studied in this series showed an orderly spoke-wheel-like arrangement of their vessels, whereas the more undifferentiated tumors revealed the characteristics mentioned above. In certain patients who have had recent fulguration of their bladder lesions, the arteriogram will show rather marked spasm of the vessels, and thus prevent proper evaluation of the true extent of the lesion.

The authors include 1 table and 2 figures to illustrate this article.—*George W. Chamberlin, M.D.*

Abrams, Herbert L., Boijsen, Eric, and Borgström, Karl-Erik. Effect of epinephrine on the renal circulation: angiographic observations. *Radiology*, Dec., 1962, *79*, 911–922. (From: Departments of Radiology, Stanford University School of Medicine, Palo Alto, Calif., and the University Clinics, Lund, Sweden.)

Malignant tumors in various locations frequently present atypical blood vessels on angiography which are a combination of normal vessels and embryonic vessels, the walls of which are devoid of elastic tissue. There is suggestive evidence that these vessels will not respond to humoral agents which characteristically affect normal blood vessels. Therefore, if it were possible to narrow adjacent normal vessels by suitable humoral agents, a redistribution of contrast agent might allow more dependable angiographic demonstration. Also, if this effect were accomplished it might be possible to perfuse a regional vascular bed with a chemotherapeutic agent, allowing a higher concentration in the tumor bed than in the surrounding normal tissues.

As a first step in clarifying this problem the authors present a study of the effect of specific pharmacologic agents on the renal vessels. Six mongrel dogs were studied angiographically with renografin as the contrast agent injected into either the renal artery or the aorta adjacent to the orifices of the renal arteries. The pharmacologic agents evaluated included: epinephrine, in doses of 5 to 50 μg./kg.; hydergin (a vasodilating drug consisting of hydrogenated ergot alkaloids) using 20 μg./kg.; and ephedrine in amounts of 4 mg./kg.

The epinephrine effect, as shown by this study, presents interesting angiographic features. In the animals studied there was dilatation of the proximal portion of the renal artery, while a striking and persistent localized zone of narrowing was demonstrated at or near the bifurcation of the renal artery. The appearance is essentially that of the authors' term, "sphincteric zone." The resistance at this zone could be overcome by increases in injection pressure, but distal segments of localized narrowing were then apparent. In addition, the diameter of the aorta increased and the time of disappearance of the medium from the aorta also increased, while the nephrogenic phase was prolonged but decreased in intensity. Evaluation of the other drugs disclosed that hydergin, given 60 seconds after epinephrine, almost completely abolished the epinephrine effect while ephedrine did not significantly affect renal vessels or renal blood flow from an angiographic standpoint.

This study confirms the presence, in dogs, of a local sphincteric action in the major renal arteries in response to the administration of epinephrine, in a minimal dose of 5 μg./kg. These observations suggest that the site of major resistance to flow may be extrarenal rather than intrarenal and, if so, then its use as a means of selectively distributing chemotherapeutic agents or contrast media is not feasible. It remains to be shown whether a lower dosage range can be sharply defined by arteriographic techniques. The authors additionally comment that a similar "spasm" of the renal artery has been observed in clinical subjects during catheter manipulation, suggesting that the renal artery in man may respond to irritation of its wall as does the renal artery of the dog to epinephrine.—*Edward B. Best, M.D.*

Kaufman, Joseph J., Schanche, Arthur F., and Maxwell, Morton H. Excretory urography in the diagnosis of renovascular hypertension: methods of enhancing its value. *J. Urol.*, Mar., 1963, *89*, 498–505. (From: Department of Surgery-Urology and the Department of Medicine, University of California Medical Center, Los Angeles, Calif.)

Twenty-one patients with renal vascular hypertension had been studied during an 18 month period. Twenty of the 21 patients with main stem lesions and 3 of the 5 patients with segmental lesions showed roentgenographic evidence which indicated the site of the lesion in the kidney.

An evaluation of the kidney size is helpful but is not completely diagnostic in the determination of renal vascular hypertensive etiology. In comparing kidney size one must recognize that the left kidney is normally larger than the right so that a small diminution in the size of the left kidney may be of significance when compared with the size of the right kidney. Furthermore, the normal kidney mass may contract during anesthesia or in response to medication during the nephrogram phase which might produce an error in evaluation of renal size.

Changes in the contour of a segmentally ischemic kidney are difficult to detect, but when present, segmental atrophy may be of sufficient significance to call one's attention to a lesion involving a branch of the renal artery.

Difference in filling of the calyceal system is not an entirely reliable sign in itself, but when combined with other findings, it is of some significance. Only 7 of 20 cases of main stem lesions and 2 of 5 segmental lesions as recorded by the authors have shown measurable differences in calyceal filling. Pyelograms made under conditions of hydration will often accentuate the difference in calyceal filling, whereas with dehydration the collecting systems of both kidneys will be carrying a small volume, and hence both may appear contracted. With hydration, the normal side will be better filled than the ischemic side.

Differences in the concentration of the contrast medium will depend upon the state of hydration of the patient. During dehydration, pyelography may fail to demonstrate any changes on the two sides even though one side may be ischemic and the other side normal. However, if one hydrates the patient moderately, the ischemic side may show increased density due to increased tubular resorption. In this respect it must be remembered that overhydration will unfavorably affect the technical quality of the pyelograms and should be avoided.

One of the most valuable single roentgenographic procedures is the use of films exposed at 2, 3, and 5 minutes after the rapid injection of hypaque intravenously. The opaque medium should be injected in approximately 30 seconds, and films exposed promptly thereafter. On such rapid pyelograms, the appearance of the opaque medium is delayed in the ischemic segment of the kidney. In the authors' series, there was only 1 false negative appearance time in a series of main stem renal artery lesions.

There are 4 tables and 5 figures illustrating this article.—*George W. Chamberlin, M.D.*

DOIG, A., LAWRENCE, J. R., PHILP, T., TOTHILL, P., and DONALD, K. W. ^{131}I-"Hippuran" renography in detection of unilateral renal disease in patients with hypertension. *Brit. M. J.*, Feb. 23, 1963, *1*, 500–504. (From: Departments of Medicine, Radiodiagnosis and Medical Physics, University of Edinburgh, and Royal Infirmary, Edinburgh, Scotland.)

Recognition of unilateral renal disease in hypertension has become surgically important. Published reports on detection of unilateral disease with radioactive renography have been both favorable and unfavorable.

In this series 203 hypertensive patients were studied by means of both I^{131} hippuran renography and excretory pyelography.

Comparison of the pyelographic and renographic findings showed good agreement in 77 per cent of cases. Seven cases of unilateral arterial disease were found, 6 of which were detected on renography and only 3 on pyelography. Both techniques are recommended for selecting hypertensive patients for aortography and divided renal function tests.—*Bernard Loitman, M.D.*

LAWRENCE, J. R., DOIG, A., KNIGHT, I. C. S., and TOTHILL, P. Value of ^{131}I-"Hippuran" renography in urological investigation. *Brit. M. J.*, Feb. 23, 1963, *1*, 504–507. (From: Departments of Medicine, Clinical Surgery, and Medical Physics, University of Edinburgh, and Royal Infirmary, Edinburgh, Scotland.)

I^{131} hippuran renography is a simple and safe diagnostic procedure involving the recording of radioactivity over the kidneys for 10 to 15 minutes after a single intravenous injection of I^{131} hippuran.

The results obtained in 30 patients with various urologic disorders are reported.

In renal colic, ureteric obstruction is shown by delayed excretion and the subsequent course of the obstruction can be followed by serial renograms. When persistent obstruction causes impairment of renal function, this is also shown by changes in the renogram. Differentiation between anuria of ureteric obstruction and acute renal failure can be readily made.—*Bernard Loitman, M.D.*

VAN VELZER, D. A., BURGE, C. H., and MACINTYRE, R. S. Clinical evaluation of a new medium for excretory urography: a comparison study of renovist and renografin 76 per cent. *Radiology*, Dec., 1962, *79*, 939–941. (From: Department of Radiology, Methodist Hospital, Houston, Tex.)

The authors present an evaluation of a study of renovist as compared to renografin 76 per cent in routine excretory urographic examinations. Renovist is an aqueous solution of methylglucamine and sodium diatrizoate providing approximately 9.3 gm. of iodine in each 25 cc. of solution, or approximately 37 per cent iodine. It is a modification of the renografin formula with a lower viscosity, which facilitates administration.

A total of 904 patients were involved in this study with 560 patients having received renovist and 344 renografin 76 per cent. The dose of renovist was either 15, 20, or 25 cc., while the dose of renografin 76 per cent was always 20 cc. Any reactions that developed after the administration of either medium were recorded. At the completion of the study, representative roentgenograms from 633 cases were evaluated as to quality of contrast. Reactions such as pains in arm, vomiting, warmth and flushing occurred only slightly more frequently with renovist than with renografin 76 per cent, while nausea occurred slightly less frequently. There were no serious reactions to either medium in any patient in this series. Only 3 patients required any treatment because of a reaction and these were urticarial manifestations which followed injection of renovist. Good or excellent urograms were produced with both media in a high percentage of cases. The best yield was obtained with 25 cc. of renovist, but a dose of 20 cc. of this medium provided good or excellent urograms in 86 per cent of cases and diagnostic films in 95 per cent.

The authors conclude that renovist in a dose of 25 cc. is an excellent contrast medium for excretory urography and they prefer it over renografin 76 per cent, since it is more easily administered because it is less viscous. They feel that in the 25 cc. dose it provides diagnostic urograms in almost every case without appreciable increase in the low reaction rate consistently experienced with renografin.—*D. N. Dysart, M.D.*

MacEwan, D. W. Demonstration of ureteral stump reflux by voiding cystourethrography during excretory pyelography. *J. Canad. A. Radiologists*, Mar., 1963, *14*, 39–43. (From: The Montreal Children's Hospital, Montreal, Quebec, Canada.)

A survey of 81 children with partial or total nephrectomy in the last 11.5 years was made at The Montreal Children's Hospital to study the problem of ureteral stump reflux. The operations were performed for ureteropelvic obstruction in 31 cases, Wilms' tumor in 23 cases, double collecting system and infection in 13 cases, renal infection in 5 cases and for miscellaneous reasons in 9 cases.

The abnormalities that occur in the ureteral stump following partial or complete nephrectomy are poor drainage of the stump, fistula, stone formation, infection in the stump, vesico-ureteral reflux and rarely malignancy. The symptoms and signs include frequency, dysuria, pyuria, hematuria, ureteral colic, abdominal pain, attacks of fever, persistent wound drainage and fistula.

It would be very helpful if there were an accurate method of predicting in advance those children in whom it would be desirable to remove the ureter completely at the initial operation. The author believes that voiding cystourethrography before removal of the kidney and ureter would establish the presence or absence of reflux. If ureteral reflux is present these children should be considered for complete ureterectomy at the time of the initial surgery. Voiding cystourethrography is valuable at the time of excretory pyelography and has many advantages. It appears to be equally reliable as retrograde cystography and its simplicity allows it to be used as a screening procedure.

The author reports 1 case in which reflux into the ureteral stump caused pain, 2 cases in which infection resulted, and 2 cases in which no difficulty occurred. In the author's experience the children with double collecting systems and urinary infection are the ones who may have subsequent trouble from ureteral stump reflux.—*J. N. Ané, M.D.*

SKELETAL SYSTEM

Bywaters, T. W., Jr., Bailey, R. W., Carroll, C. J., and O'Connor, G. A. Infantile cortical hyperostosis presenting with exophthalmos: case report. *J. Michigan M. Soc.*, Mar., 1963, *62*, 285–288. (From: Department of Surgery, Section of Orthopaedics, University of Michigan Medical Center, and St. Joseph Mercy Hospital, Ann Arbor, Mich.)

In 1939 Caffey observed periostitis in an infant which was not explained by the known disease entities. Caffey and Silverman in 1945 reported 4 cases and coined the term "infantile cortical hyperostosis."

The clinical course typically begins in an infant 5 months or less of age. The average age of onset is 9 weeks. The infant presents with irritability, low grade fever, leukocytosis, elevated sedimentation rate, mild anemia and pallor. Anorexia and mild diarrhea may occur. Swelling appears early in the course and rather suddenly; it is brawny or woody hard.

Pseudoparalysis may occur and pleurisy with or without pleural effusion may be present. Local tenderness develops early but local warmth, discoloration, hyperemia or lymphadenopathy appear later. Bona fide cases apparently do not have their time of onset after 5 months.

The etiology has not been established.

Roentgenographically there is evidence of varying amounts of immature bone deposited about the diaphysis of a long bone between, but not involving, the epiphyseal plates. Recovery takes place by medullary widening and reduction in thickness of the cortical bone from within. Subsequently remodelling with a decrease in the diameter of the diaphysis to normal occurs. Residual is uncommon although synostosis of radius, ulna and adjacent ribs is observed.

The clinical signs generally disappear by the age of 1 year and the roentgenographic evidence by the end of 3 years.

The sites of involvement include all tubular and flat bones, although involvement of the vertebrae, phalanges, carpal and tarsal bones has not been reported. The most common sites are the mandible, clavicle and ulna with frequent occurrence in the frontal and parietal bones, facial bones, ilia or a single scapula.

A case is reported of a Negro male who first presented with exophthalmos and swollen eyelids at 6 weeks of age. At 14 weeks swelling of the right leg was noted; it was hard and nontender. Roentgenograms of the skull demonstrated apparent thickness of the cortical bone of both orbits. The right tibia and fibula showed diffuse periostitis. At 4½ months swelling was noted about the mandible and periosteal new bone was evident on the roentgenograms. Subsequent visits revealed no new manifestations. At 9 months roentgenograms of the skull and right tibia showed partial resolution of the previous changes.—*David Morse, M.D.*

Scott, Thomas F., and Bailey, Robert W. Idiopathic scoliosis in fraternal twins. *J. Michigan M. Soc.*, Mar., 1963, *62*, 283–284.

(From: University of Michigan Medical Center, Ann Arbor, Mich.)

Scoliosis in twins has been studied with interest in regard to a possible clue to the pathogenesis. All cases but one studied at the University of Michigan Medical Center have been in identical twins. This report concerns scoliosis in proven fraternal twins.

Cases reported in identical twins as well as the case presented here have several characteristics in common: (1) they usually fall into the adolescent or preadolescent grouping; (2) the primary curves are dorsal or dorsal-lumbar; (3) the heavier twin usually has the larger curve; and (4) all cases reported have been in girls.

The scoliosis in the fraternal twins was 45 degrees dorsal-lumbar in the lighter twin and 50 degrees lumbar-sacral in the heavier twin. Some progression of the curves was present in the 3 months follow up. Utilizing Cook casts and two stage spinal fusions with homogeneous bone grafts, correction of nearly 20 degrees was achieved in both.—*David Morse, M.D.*

Epstein, Joseph A., Epstein, Bernard S., and Lavine, Leroy S. Cervical spondylotic myelopathy. *A.M.A. Arch. Neurol.*, Mar., 1963, *8*, 307–317. (Address: Joseph A. Epstein, The Long Island Jewish Hospital, 270–05 76th Street, New Hyde Park, L.I., N. Y.)

Fourteen patients with symptoms of cervical spinal cord and nerve root compression caused by osteophytes are reported. Foraminal constriction contributed to the pathology by fixation of the nerve roots with tethering of the spinal cord against the ventral ridges. Compression of the cord was caused by constriction of the neural canal both ventrally and dorsally due to proliferative bony spurring. The noncalcified portion of the spur also contributed significantly to the compression.

Individuals with congenital or developmental narrowing of the cervical canal are rendered susceptible to spondylotic myelopathy because of the diminished available space. However, it is apparent that multiple factors contribute to the pathology. A promising 80 per cent rate of significant improvement has followed decompression by laminectomy and removal of spurs. The authors feel that section of the dentate ligaments is unnecessary.—*Arch H. Hall, M.D.*

Vallebona, D. Osteofitosi e sindesmofitosi. (Osteophytosis and syndesmophytosis.) *Radiol. med.*, Mar., 1963, *49*, 209–237. (Address: Via Brigate Partigiane 18/5, Genova, Italy.)

The author considers four pathologic entities in which osteophytes and syndesmophytes, or calcified paraspinous ligaments, are to be found: (1) spondylarthrosis; (2) spondylarthrosis with tendency to ankylosis; (3) senile vertebral ankylosing hyperostosis of Forestier; and (4) ankylosing spondylitis.

In the first group, the osteophytes of spondylosis are seen mainly on the right side and in the thoracic spine; and to a lesser extent in the lumbar spine, anteriorly. This is due to the effect of the thoracic aorta on the dorsal spine, as postulated by Culver and Pirson and others.

In the second group are cases in which the osteophytes form bony bridges, primarily located in correspondence with the thoracic segment of the spine.

In the third group, senile vertebral ankylosing hyperostosis, one notes a moderate kyphosis and bony bridges localized mainly in the lower segment of the thoracic spine, anteriorly and laterally, on the right side. On the left side one notes only plain osteophytes.

In the fourth group, ankylosing spondylitis, the roentgen findings are well known.

It is pointed out, in particular, that in the initial stages when a differential diagnosis could be difficult to make, the development of syndesmophytes is not influenced by the position of the aorta, as is in the case of the osteophytes.—*A. F. Govoni, M.D.*

Wells, L. H. Congenital deficiency of the vertebral pedicle. *Anat. Rec.*, Feb., 1963, *145*, 193–196. (From: Department of Anatomy, University of Cape Town, Republic of South Africa.)

Partial absence of the vertebral pedicle appears to be decidedly uncommon. Two instances of unilateral absence of pedicle occurring in a single sacral vertebra and a third instance of a partially absent pedicle of a fifth lumbar vertebra are reported from the Anatomy Department, University of Witwatersrand, Johannesburg.

Three examples of similar involvement are cited from the literature, and the possible mechanism of development of such anomalies is discussed.—*Lois C. Collins, M.D.*

Mead, Charles A., and Martin, Mildred. Aplasia of the trochlea—an original mutation. *J. Bone & Joint Surg.*, Mar., 1963, *45A*, 379–383. (Address: 836 Miami Road, Jacksonville, Fla.)

Various elbow anomalies have been described but the authors did not find any cases similar to these in a review of the literature.

Five cases of an unusual elbow deformity in a mother and 4 of her children are reported. One of these died in infancy and is said to have had elbow deformity; the other 4 patients all showed similar bilateral changes.

The elbow is held in flexion with extension possible to 90 degrees and flexion to 30–60 degrees. The humerus is short, and a web of soft-tissue stretches across the antecubital space. The medial portion of the humerus is deformed with no trochlea or medial epicondyle present. The ulna is dislocated medially and proximally and does not articulate with the humerus. The radial head articulates with the capitellum.

The genetic consultant at Tulane University stated that the condition was caused by an autosomal dominant gene. Affected individuals would be expected to transmit it to one half their offspring and unaffected individuals are not expected to be carriers. —*Martha Mottram, M.D.*

PAUS, BERNHARD C., and KIM, TAK KI. Osteoid osteoma of the spine. *Acta orthop. scandinav.*, Jan., 1963, *33*, 24–29. (From: Department of Orthopaedics of the National Medical Center in Korea.)

The authors feel that about 10 per cent of osteoid osteomas are localized to the spine usually in the lamina, the facets or the processes. They report the case of a 21 year old male who had suffered from back pain for 5 years which eventually incapacitated him. Roentgenograms revealed a density in the right side of the body of L4 with a sharply defined central defect. In the center of this defect there was an irregularly calcified area. Operation revealed a typical osteoid osteoma. The patient returned to full time work within 3 months and roentgenograms 7½ months later showed no residual defect.

The case is considered unusual because of the location of the lesion in the vertebral body.—*Arthur E. Childe, M.D.*

FRIEDENBERG, Z. B. Protrusio acetabuli in childhood. *J. Bone & Joint Surg.*, Mar., 1963, *45A*, 373–378. (Address: 3400 Spruce Street, Philadelphia 4, Pa.)

Inward protrusion of the femoral head into a deepened acetabulum may be the result of a specific disease process such as Paget's disease, rheumatoid arthritis, osteomalacia or trauma. It is also seen as a primary process; in these instances it is more common in adolescents and young women, usually bilateral, and later in life is associated with an osteoarthritis.

For the diagnosis there must be a deepened acetabulum as well as an inward displacement of the femoral head. The CE angle of Wiberg is used by the author to measure the inward protrusion; in normal adults this ranges from 20 to 46 degrees with an average of 26 degrees; in children (6–13 years) the range is 15 to 40 degrees with an average of 30 degrees.

Two cases are reported aged 8 and 11 years. Both had a painful limp. Roentgenograms showed bilateral protrusio acetabuli. One patient had unilateral arthrotomy which revealed normal capsule and articular cartilage with thickened synovia. There was little progression in either case by age 18 and the patients were relatively asymptomatic. Both showed early fusion of the capital epiphyses.—*Martha Mottram, M.D.*

WRAY, JAMES B., and HERNDON, C. NASH. Hereditary transmission of congenital coalition of the calcaneus to the navicular. *J. Bone & Joint Surg.*, Mar., 1963, *45A*, 365–372. (From: Bowman Gray School of Medicine, Winston-Salem, N. C.)

Talocalcaneal bar, which is an osseous or fibrous union of the talus to the calcaneus, usually produces pain and disability of the foot. Special roentgenographic projections are necessary to show it. Coalition of the calcaneus with the navicular by fibrous or osseous bridge is easier to recognize roentgenologically and is generally apparent in a standard view of the foot. However, this lesion may normally exist without clinical symptoms.

The authors report the case history of a 37 year old man who had bilateral coalition of the navicular with the calcaneus. It was found that his 13 year old son also had foot trouble and roentgenograms demonstrated the same type of lesion. Following this, the authors began to examine the rest of the family and discovered that the original patient's father likewise had this type of deformity.

Excellent roentgenographic reproductions are included showing the defect in great detail.

The authors hazard the opinion that at least some and perhaps all cases of calcaneal-navicular bar are caused by specific gene mutation which behaves as an autosomal dominant. The examination of relatives of patients with this defect should prove to be rewarding and furnish needed information concerning the cause and distribution of the defects.—*David Alftine, M.D.*

STEIN, ARTHUR H., JR. The relation of median nerve compression to Sudeck's syndrome. *Surg., Gynec. & Obst.*, Dec., 1962, *115*, 713–720. (From: The Orthopedic Division of the Department of Surgery, Washington University School of Medicine, St. Louis, Mo.)

Sudeck's syndrome occurs most commonly after an injury to the wrist. It is characterized by severe pain and swelling of the hand and often of the forearm. Hyperemia is present in the early stage. Limitation of motion is marked in the wrist and fingers, while the elbow and shoulder are affected to a lesser extent. As the acute phase subsides the hand becomes atrophic, cool, cyanotic and stiff.

Roentgenographically there is rapid severe demineralization of the bones of the wrist and hand. This is most marked in the metaphysis of the long bones and in the carpal bones. The diaphysial portion of the long bones is relatively spared.

The true cause of the condition is not known but the author observed 6 personal cases which all had an anatomically demonstrated irregularity of the median nerve as it passed through the volar carpal tunnel. All cases showed marked improvement after decompression of the median nerve. The visible alteration consisted of fine adhesive bands binding the nerve to the tendons within the volar carpal tunnel.

The author suggests that the surgeon should search for a local median nerve irritation in this clinical syndrome.—*H. R. Hittner, M.D.*

Jeffreys, T. E. The painful heel in adolescence. *Brit. J. Surg.*, Nov., 1962, *50*, 327–329. (From: Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, England.)

This article is based on a review of 8 patients, ages 11 to 24 years, seen at the Robert Jones and Agnes Hunt Orthopaedic Hospital. It describes a syndrome, occurring in adolescents, in whom a painful heel is associated with cysts of the calcaneum. In 3 patients the diagnosis of chronic inflammatory cysts was apparent. Of the other 5 cases, 2 were shown to be of a chronic pyogenic nature, 1 was an osteoid osteoma and in 2 cases the histologic examination did not establish a diagnosis.

Roentgenographic reproductions illustrate the typical appearance.

In the majority of the cases studied the cyst was actually a chronic abscess cavity. Fracture may occur through the cyst. One of the cases had cysts of the right and left calcaneum. This patient had worn crooked and elongated heels for correction of bilateral flat feet.—*C. B. Frydenlund, M.D.*

Denham, R. H., Jr., and Dingley, A. F., Jr. Fibrosarcoma occurring in a draining sinus. *J. Bone & Joint Surg.*, Mar., 1963, *45A*, 384–386. (Address: 919 East Jefferson Boulevard, South Bend 17, Ind.)

This is a case report of a patient who had 2 fractures of the left femur with open reduction 20 years previously. There was persistent drainage which gradually increased, with development of a fungating mass 5 cm. in size, on the lateral aspect of the thigh at the upper end of the draining sinus.

Amputation was done. The tumor mass invaded the bone. The pathologic diagnosis was well differentiated fibrosarcoma and chronic osteomyelitis.—*Martha Mottram, M.D.*

Dragoni, G., and Salvini, E. Studio clinico-radiologico del plasmocitoma; (considerazioni su 43 casi). (Clinical and radiologic study of plasmocytoma; [considerations of 43 cases].) *Radiol. med.*, Feb., 1963, *49*, 97–126. (Address: Dott. Prof. Giovanni Dragoni, Orio Litta, Milano, Italy.)

From the case material of the Department of Radiology of the University of Milan, Division of Radiology of the National Institute for the Study and Treatment of Tumors, the authors selected 43 cases of plasmocytoma which were studied clinically and roentgenologically and were all verified histologically.

In reviewing the roentgen findings, the clinical picture and the laboratory data, it appeared that there was no relationship between the laboratory data, specifically the electrophoretic patterns, the degree of skeletal involvement and the clinical findings.

In 8 cases the plasmocytoma was of the solitary type and it remained so for the duration of the disease. In 3 cases, although multiple biopsies and bone marrow studies demonstrated the presence of plasmocytoma, several roentgen studies of the skeleton failed to reveal any bone involvement.

The treatment, surgical or radiotherapeutic, pharmacological or purely symptomatic, has been applied in accordance with the site, extension, and dissemination of the disease and the general condition of the patient. The results have been rather poor and only the subjective symptomatology of the individual was improved.

Radiotherapy has been of a certain advantage in cases with limited and localized skeletal involvement, or in solitary extraskeletal lesions.—*A. F. Govoni, M.D.*

Bose, K. S., and Chowdhuri, B. Observations on synovial sarcoma. *J. Indian M. A.*, Dec., 1962, *39*, 621–627. (From: Orthopaedic Department and Pathology Department, Medical College, Calcutta, India.)

Ten cases were studied during the period 1957–1961. These were encountered in about 80,000 new patients seen during that time, indicating the rarity of the condition. The roentgenologic features were most pronounced probably due to the advanced stage of the disease in this series. These features included: Soft tissue swelling near a joint in all cases; scattered areas of calcification; pressure atrophy of bone; osteolytic erosion of bone; periosteal reaction; pathologic fracture and decalcification. Bone involvement occurred in 70 per cent leading to erroneous roentgenologic diagnosis of osteomyelitis, tuberculous arthritis, osteogenic sarcoma, etc. Incisional biopsy for arriving at a definite diagnosis is stressed.

The incidence rate was 0.0008 per cent, with an average age of 37.1 years, and male to female ratio of 9:1. All cases were in the lower extremity. The results of adequate treatment seemed better than obtained with osteogenic sarcoma. Longer survival was seen in those cases having mature fibrous tumor stroma.

Short duration of symptoms carried a poor prognosis.—*Richard E. Kinzer, M.D.*

Vose, George P. Fine structure of bone as seen on fracture and cleavage planes by electron microscopy. *Anat. Rec.*, Feb., 1963, *145*, 183–192. (From: Nelda Childers Stark Laboratory, Texas Woman's University, Denton, Tex.)

The submicroscopic structure of bone, the structural morphology between the crystalline and canalicular levels, can be studied by electron microscopy.

Surface replicas of fracture surfaces and cleavage planes of specimens of the anterior cortex of femur of 2 adults and 1 twelve year old girl were examined by electron microscopy after fractures were produced by compression, torsion, tension, or bending. This method permitted study of the canalicular structure and pattern of complex fibrous systems which radiate from the canaliculi.

No differences were observed in the submicroscopic unit structure of young and old bone, or of the bones fractured by the different types of stress.—*Lois C. Collins, M.D.*

Blood and Lymph System

Goffrini, Piero. L'injection radio-opaque du canal thoracique: observations morphologiques et fonctionnelles sur la circulation lymphatique lors des blocages néoplasiques des ganglions lymphatiques sous-diaphragmatiques et médiastinaux. (Radiopaque injection of the thoracic duct: morphologic and functional observations on lymphatic circulation when the subphrenic and mediastinal lymph nodes are blocked by neoplastic involvement.) *Presse méd.*, Dec., 1962, *70*, 2751–2754. (From Institut de Pathologie spéciale chirurgicale et propédeutique, Clinique de l'Université de Parme, Parma, Italy.)

The author compares two methods of opacification of the thoracic duct: the retrograde lymphography and the ascending lymphography.

In the first method, injection of a hydrosoluble substance is made under low pressure at a rate of 3–4 cc. per minute to avoid rupture or modification in the permeability of the vessel wall. Roentgenograms are taken 1 minute after injection and then every 30 seconds for 4 minutes. The first roentgenograms are centered over the thorax, the others over the abdomen in anteroposterior and lateral projections. Intubation of the thoracic duct results in its definite interruption, except when the caliber is large and the walls resistant, permitting re-establishment of its continuity. The ligature of the duct does not produce subjective or objective embarrassment because of the existing collateral drainage (right paratracheobronchial chain to supraclavicular fossa, paravertebral lymphatics to azygos system).

This method is still experimental, antiphysiologic, and inadequate for functional studies. Roentgenologically, the significant findings, although not completely convincing, consist of: (1) retrograde opacification of dilated collaterals (normally valvular structures prevent the retrograde injection); (2) demonstration of enlarged lymph nodes which are nonpermeable or show irregular opacification with irregular defects; and (3) interruption of the duct at different levels corresponding to intrinsic neoplastic involvement.

In the second method, ultrafluid oily contrast material is injected in the lymphatics of one or both feet which gives a high concentration in the abdominal lymphatics. The injection is done at a rate not more than 1 cc. per 10 minutes for a total of 8 to 10 cc. in each foot. In the author's experience, the chronologic sequence of the opacification by this method is rather constant: 15 minutes after the completion of the injection, the abdominal portion of the duct is visualized and, in ideal cases, it is shown in all its length for 30 to 90 minutes. Then, the opaque column becomes fragmentary and disappears in 2 hours. The examination is completed by taking other roentgenograms 24 hours later and on the days following for study of the lymph nodes.

The second method is more physiologic and permits evaluation of the lymph flow in the duct revealing stasis or increased flow. The visibility of the duct depends on the amount of the injected material and its endolymphatic concentration. Repeated roentgenograms are necessary at 30 to 120 minutes because the thoracic duct opacification is variable and subject to the influence of respiratory movements. Normally early and dense opacification of the duct is due to a rapid flow; the opposite characterizes stasis. When the lymph nodes are enlarged (iliac and lumbar-aortic), as seen in lymphoma and hyperplastic conditions, the duct is opacified tardily and the injected column is fragmentary or partially missing.

On the other hand, the duct is seen clearly and early if numerous lymph nodes are invaded by cancer, although massive invasions of the lymph nodes and vessels causing stasis and blockage can prevent opacification of the thoracic duct.

Normally, the lymph nodes are opacified to the level of the second lumbar vertebra. When the obstruction is above the diaphragm, some lymph nodes are opacified above the second vertebra, probably due to a subdiaphragmatic stasis. With partial or total blockage along the thoracic duct, a prolonged opacification may be seen, with an increased number of tributaries and opacification of the lymph nodes which normally do not drain into the thoracic duct (lymph nodes of the tracheal bifurcation; paratracheal, paravertebral and intercostal lymph nodes); their opacification, however, is very faint, probably because they have lost their filtrating function and their role as collateral vessels.—*H. P. Lévesque, M.D.*

Pelkey, W. J., Powell, P. R., and Fagan, W. T. Experiences with lymphangiography. *J. Urol.*, April, 1963, *89*, 611–614. (From: Division of Urology, Department of Surgery, College of Medicine, University of Vermont, Burlington, Vt.)

The technique for this procedure consists of the injection of 0.1 cc. of a mixture of 75 per cent direct sky blue and 25 per cent of 1 per cent xylocaine into the skin between the toes. Approximately 30 to 45 minutes later, a small G-shaped skin flap is elevated on the dorsum of the foot. By careful dissection of the subcutaneous tissues, 1 to 4 lymphatics are visualized for a 1½ to 2 cm. distance. A single ligature of 6.0 arterial silk is passed around the lymphatic structure. As traction is applied to the ligature, a special needle connected to polyethylene tubing is introduced into the lymphatic vessel under the Zeiss binocular operative microscope. After the needle has been threaded approximately 0.5 cm. into the lymphatic vessel, it is secured with the arterial silk suture. The apparatus is then connected to a constant-speed Harvard pump which supplies ethiodol at a constant speed. An infusion rate from 0.2 to 0.8 cc. per minute has been found to be satisfactory. Warming the ethiodol to body temperature reduces its viscosity and aids in the administration of the opaque medium. Approximately 15 minutes after injection has begun, a scout roentgenogram of the calf of the leg is taken to demonstrate opaque medium in the lymphatics. If opacification of the lymphatics is not demonstrated, it is assumed that local extravasation has occurred and the other lymphatics are then exposed for cannulation.

The authors include 4 brief abstracts of clinical records of patients in whom this study was performed. The use of the binocular operating microscope ensures 100 per cent certainty that the vessel being cannulated is a lymphatic instead of a venous one, and the special needle used by the authors provides an extremely small gauge which can be securely fastened to a short section of polyethylene tubing. The use of the constant-speed Harvard pump helps to obviate extravasation and rupture of the lymphatics since it offers a steady infusion rate dependent upon the pressure within the lymphatics.

Six figures are used to illustrate this article.—*George W. Chamberlin, M.D.*

Wohlgemuth, J. A simple injector for lymphangiography. *Radiology*, Feb., 1963, *80*, 251. (From: University Hospital, Baltimore, Md.)

A simple and inexpensive gravity feed device to serve as an injector for lymphangiography is described. A large block of wood is bored to hold two 10 cc. syringes. Two strap hinges are attached to the block so that they will form a 90° angle when the syringe is at the 5 cc. level. Lead weights are placed upon the lever, and their position may be varied to change the rate of flow of the contrast medium. The large block of wood is supported by two smaller blocks which permits clearance of the tip of the syringe and its attached tubing.

The article includes an illustration of the described device.—*Ralph F. Bowman, M.D.*

Bron, Klaus M., Baum, Stanley, and Abrams, Herbert L. Oil embolism in lymphangiography: incidence, manifestations, and mechanism. *Radiology*, Feb., 1963, *80*, 194–202. (From: Department of Radiology, Stanford University School of Medicine, Palo Alto, Calif.)

Lymphangiography is proving to be an important diagnostic method in studying the lymphatic network. The authors discuss one of the complications, ethiodol pulmonary embolism, as encountered in their series. Their technique was that of Kinmouth as modified by Wallace, using warmed ethiodol delivered by an automatic injector at the rate of 12 cc. per hour, 10 cc. per lower extremity, with a total maximum of 20 cc. Fluorographic and roentgenographic monitoring are considered an essential part of the examination.

In 44 of 80 patients (55 per cent) pulmonary ethiodol embolization was encountered. Of those having embolization, lymphatic obstruction was apparent in 31. There were 7 patients who had obstruction who did not have embolization. Symptoms and signs of embolization were usually mild, with chills, slight fever, cough, pleuritic pain, and mild to moderate dyspnea. Some patients were asymptomatic, while 2 debilitated patients had severe reactions including hypotension and electrocardiographic evidence of right heart strain. The roentgenologic evidence of embolization was manifested within the first 12 hours. There was fine granular stippling throughout both lung fields, although occasionally a linear or reticular pattern was visible. Frequently the roentgen changes preceded any clinical symptoms. Therapy is supportive and nonspecific. Clinical recovery is usually complete in 48 to 72 hours.

The authors noted that the embolization was similar to that seen in patients who had venous intravasation with oily contrast media during hysterosalpingography. They then used dogs to show that ethiodol stayed in the lymph channels when there was no obstruction, but went into the venous channels when the usual channels were obstructed. This produced the same type of embolization as is occasionally seen with hysterosalpingography. It is felt that this observation on dogs can probably be applied to man, although this does not preclude other forms of embolization. Likelihood of embolization can be reduced by careful monitoring and discontinuance of the injection as soon as obstruction is noted. Development of an aqueous medium which is capable of demonstrating para-aortic lymph nodes would be the best preventative.—*James C. Moore, M.D.*

GENERAL

HALL, P. Albright's syndrome in an adult male: report of an atypical case with psychiatric symptoms. *Brit. M. J.*, Nov. 3, 1963, *2*, 1159–1161. (From: The Department of Psychiatry, University of Sheffield, Sheffield, England.)

This syndrome of unilateral cutaneous melanosis, polyostotic fibrous dysplasia, and precocious puberty is of unknown etiology. Only a small number of males have been reported; and of these, few have had the complete syndrome, few have been adults, and none has been fertile. The diagnosis is not difficult and the discovery of the condition may obviate possible parathyroid surgery.

The case reported concerns a 30 year old male with skin, bone, and testicular abnormalities which played a part in the development of a neurosis; this led to his hospitalization. He had previously had two operations for a suspected parathyroid adenoma based on roentgenographic findings of osteitis fibrosa cystica with a pathologic femoral fracture. Current roentgenograms revealed sclerosis and thickening of the left facial bones and cranium, together with cystic changes in the pelvis, femora, ribs and left scapula; a large cyst involved the entire body of L4. Many laboratory tests and the results of other studies are mentioned. The serum alkaline phosphatase was 61 King-Armstrong units; the chromosome studies were normal. The disabling neurosis responded to psychotherapy.—*William H. Baker, M.D.*

MONTGOMERY, MAX M., POSKE, ROBERT M., PILZ, CLIFFORD G., BARTON, EVAN M., and FOXWORTHY, DONALD T. Reiter's syndrome. *G.P.*, April, 1963, *27*, 88–95. (From: Veterans Administration West Side Hospital, Chicago, Ill., and Veterans Administration Hospital, Hines, Ill.)

Reiter's syndrome consists of urethritis, conjunctivitis, mucocutaneous lesions and arthritis. The disease is self-limited, of unknown etiology with no specific treatment.

Arthritis is the most disabling manifestation. Unilateral or asymmetric sacroiliac involvement is seen with sclerosis and irregularity of the joint margins. However, symptoms referable to the spine are infrequent. Bony bridging of the lower lumbar vertebral bodies is found, but not the typical "bamboo spine" of rheumatoid arthritis. Destructive osteoarthropathy of the interphalangeal joints of the great toes and metatarsal heads is fairly frequent. Heel pain is often severe and may be related to a bursitis of the region.

Gonococcal arthritis, rheumatoid spondylitis and psoriasis are to be considered in the differential diagnosis but can be separated fairly easily by the clinical findings.—*Barry E. Gerald, M.D.*

PACE, WILLIAM R., JR., DECKER, JOHN L., and MARTIN, C. J. Polymyositis: report of two cases with pulmonary function studies suggestive of progressive systemic sclerosis. *Am. J. M. Sc.*, Mar., 1963, *245*, 322–332. (From: Department of Medicine, University of Washington, and the Institute of Respiratory Physiology, Firland Sanatorium, Seattle, Wash.)

Included in the diffuse collagen diseases is polymyositis or dermatomyositis when cutaneous involvement is present. Generalized scleroderma is closely related. Common to these two diseases are skin and muscle changes, calcinosis, and certain visceral lesions. Clinical, roentgenologic, pathologic, and functional findings in the lungs of patients with progressive systemic sclerosis have been reported.

The authors describe 2 cases considered to be polymyositis with diffuse pulmonary disease when first seen. One has had the disease for 9 years and the other died after 18 months. The history, clinical findings and details of the progress of the disease are given in each case. Good laboratory work-up is included and the roentgenograms of the chest, and in one instance of the hand, are reproduced.

The conclusion is reached that polymyositis may be seen as the initial phase of progressive systemic sclerosis. At this stage of the disease a combined picture of a type often noted in many of the collagen diseases is present. One patient was initially diagnosed as having periarteritis nodosa, then as having polymyositis, and at the time of the article was considered to have progressive systemic sclerosis.—*David Elftine, M.D.*

SLIM, MICHAEL S., and SIEBER, WILLIAM K. Unusual manifestations of staphylococcic infection in infants and children. *Surg., Gynec. & Obst.*, April, 1963, *116*, 387–397. (From: Departments of Surgery, Children's Hospital of Pittsburgh and the University of Pittsburgh School of Medicine, Pittsburgh, Pa.)

A critical review of 15 infants and children in whom severe and bizarre staphylococcic infection was localized, and other serious staphylococcic disease absent, is presented. In only 2 patients was the portal of entry known, in one a paronychia and in the other an infected venesection incision. Normal temperatures were consistently recorded in infants less than 2 months of age. The leukocyte count was always elevated at some time during the course of the disease, and high counts, up to 40,000, were not unusual.

Adequate specific treatment was delayed in most cases because of misdiagnosis and occasionally because of false dependence on antibiotics. Only one-fifth of the patients had staphylococcic strains sensitive to penicillin. Only after surgical exploration was the correct diagnosis reached in one-third of the cases.

Three cases of retroperitoneal abscess simulated a sacrococcygeal teratoma, retroperitoneal sarcoma, and hip joint disease, respectively. In a patient with liver abscess, antibiotic treatment without specific diagnosis undoubtedly prolonged the ailment. Two patients with pulmonary infections were treated surgically because of uncertainty of diagnosis, but it is pointed out that lung abscesses and empyema are usually controllable by intensive antibiotic treatment and surgical drainage when indicated, and lung resection is rarely necessary.

Additional sites of infection in this series were infection following inguinal herniorrhaphy, urachal abscess, retrobulbar abscess (without history of trauma or systemic infection), 3 patients with multiple infections following septicemia, and 1 patient with a parotid abscess.

Care of minor infections, restraint in the use of prophylactic antibiotics, and use of surgical drainage when indicated are stressed.—*Lois C. Collins, M.D.*

JOHNSTON, ROBERT F., GREEN, ROBERT A., and HEADINGTON, JOHN T. Progressive multifocal leukoencephalopathy. *A.M.A. Arch. Int. Med.*, Mar., 1963, *111*, 353–362. (From: Medical and Pathology Services, Veterans Administration Hospital, and the Departments of Medicine and Pathology, University of Michigan Medical Center, Ann Arbor, Mich.)

A case of progressive multifocal leukoencephalopathy, a demyelinating disease, occurring in a patient with both tuberculosis and sarcoidosis is described. The condition is characterized by progressive and fatal neurologic deterioration. The growth and histologic changes are discussed, particularly those related to the brain and spinal cord where widespread involvement is seen. The common finding is focal necrosis surrounded by irregular areas of demyelination, often with preservation of axis cylinders.

Twenty-six cases have thus far been reported, 7 in females and 19 in males. The disease is rapidly and relentlessly progressive. One patient survived for 1 year and 2 for 7 months. The rest have died within 6 months.

A definitive antemortem diagnosis of this condition cannot be made without brain biopsy, although it can be suspected if rapidly progressive neurologic disease occurs in a patient with lymphoblastoma, carcinoma, or granulomatous disease.

The cause of progressive multifocal leukoencephalopathy is unknown, but hypersensitivity or an autoimmuned mechanism is postulated.—*Francis P. Shea, M.D.*

WATSON, JOHN C., WEINSTEIN, AARON S., and GREENSPAN, RICHARD H. Advantages of three-phase spot-film radiography. *Radiology*, Dec., 1962, *79*, 973–978. (From: Department of Radiology, Yale University School of Medicine, and Radiology Services, Grace-New Haven Community Hospital, New Haven, Conn.)

The usual fluoroscopic and roentgenographic unit in this country is powered by a single phase generator. Fluoroscopy is done on the small focal spot, and spot-filming is done only on the large focal spot which is usually 2 mm. in diameter.

The authors used wire mesh embedded in plastic to demonstrate increased versatility and better roentgenograms were obtained by the use of the three phase equipment. Smaller focal spots can be used with this equipment and the roentgen tubes can be loaded to nearer their true capacity. In various combinations this can produce a much shorter exposure time, and/or better roentgenographic detail. Exposure time can sometimes be reduced to one fourth that required by single phase equipment.

The authors contrived an interesting "spinning-top" device to show both exposure times and impulses. Single phase equipment produces a series of dots on the film, while three-phase roentgenography shows a streak, thus pointing up the nearly constant-potential effect achieved with this technique.—*James C. Moore, M.D.*

RADIATION THERAPY

WATSON, T. A., and CAMPBELL, JAMES M. (Saskatoon, Saskatchewan, Canada.) Supervoltage radiation therapy in advanced cancer of the urinary bladder. *J. Canad. A. Radiologists*, Mar., 1963, *14*, 4–9.

The treatment of cancer of the bladder depends on the extent, site and histologic type of the tumor. Low-grade papilliferous cancer, which does not infiltrate beyond the mucosa, is usually effectively eradicated by transurethral fulguration. Small ulcerating or solid carcinomata, which may infiltrate the underlying muscle, are treated fairly satisfactorily by partial cystectomy or some type of radioactive source implantation at cystotomy, depending on the site. When, however, the tumor is large and penetrates deeply or extends outside the bladder, treatment becomes difficult. Total cystectomy carries with it considerable hazards in respect to morbidity and mortality. The end results are frequently unsatisfactory.

The use of external orthovoltage radiation therapy has never received wide acceptance, due to the severe reactions involved and the poor results.

The patients selected for treatment by the authors have been drawn from the Saskatoon and Regina Cancer clinics.

In the period 1949 to 1958, 131 patients were started on supervoltage therapy. In 12, treatment was discontinued before two-thirds of the proposed course had been completed because of deteriorating general condition. Males outnumbered females by 97 to 22 and ages varied from 33 to 84 years, with an average of 66.5 years. Previous surgery had been performed in the majority. This consisted of one or more transurethral resections in 47 patients, a cystotomy or laparotomy, sometimes with open fulguration, in 24, a partial cystectomy in 13, and radon seed implantation in 2. All had recurrent or residual disease at the time of supervoltage radiation therapy. Transurethral biopsy only had been performed in the remaining 33 patients. Those who had known distant metastases were not treated. Local extension or spread of the disease into the pelvis was not considered a contraindication.

The technique employed with the Co^{60} apparatus almost always consisted of anterior and posterior conical rotation at 40° incidence. The source tumor distance was always 96 cm., the size of the fields at the tumor varying from 7.2 to 12 cm. square. The actual treatment over-all time varied from 17 to 24 days. The central dose received was from 5,300 to 5,800 rads.

Systemic radiation reactions are virtually absent in this type of treatment, owing to the comparatively low integral doses involved.

The main problem has been the management of cystitis, bladder irritation and spasm. Cystitis is always present originally, because of tumor ulceration. Frequently, partial obstruction of the ureter mouths gives rise to pyelitis and sometimes pyelonephritis. Treatment was occasionally discontinued temporarily to allow the inflammation to settle down. In some cases severe cystitis continued after treatment until death. Increased frequency of micturition or mild symptoms of cystitis developed or became worse during treatment in 40 patients; 29 suffered from severe dysuria and bladder spasms.

Two patients died before treatment was completed with perforation of the bladder—presumably due to necrosis of tumor. Four patients subsequently had transplantation of ureters to the bowel.

The gross 3 and 5 year survival rates were 30 per cent and 22 per cent. In all, there are 21 five year survivors out of a total of 94 patients treated more than 5 years ago. In only 1 case was the tumor apparently confined to the mucosa, the diagnosis being multiple recurring malignant papillomata.

Postmortem examinations were performed in 48 cases. In over 40 per cent no residual tumor was found in the pelvis; of these, death was ascribed in 7 cases to the sequelae or treatment (or cancer), such as bilateral stenosis of the ureters with pyelonephritis and uremia.

In many of the cases obstruction of the ureters and ascending infection were lethal factors. More attention should be paid to ureteral diversion before and particularly after treatment in certain cases. This approach would seem preferable to total cystectomy in patients in whom the tumor has extended through the bladder wall, since it is sometimes successful. Subsequently total cystectomy can still be attempted in cases of failure.—*Stephen N. Tager, M.D.*

Jacobs, Lewis G. Unusual case of late post-irradiation damage to the ileum. *Radiology*, Jan., 1963, *80*, 57–61. (From: Veterans Administration Hospital, Oakland, Calif.)

Radiation damage to the ileum is of two types: (1) acute, usually observed during the course of irradiation or just following it, and (2) late, generally developing 6 months to 5 years after therapy. Occasionally cases of radiation damage occur much later than 5 years. This may lead to a mistaken diagnosis of recurrent neoplasm. Peterson and Clauson are reported to have estimated that, with orthovoltage therapy, acute mucosal damage may occur with 2,500 r, while 5,500 r to the retroperitoneal area will cause late radiation injury to the small intestine in about half the cases. Most reported cases were treated in the orthovoltage range. Primary diseases for which irradiation was given in such cases included: carcinoma of the cervix uteri, testicular tumors, carcinoma of the colon, carcinoma of the ovary, and plasma cell myeloma The roentgenologic diagnosis of radiation damage to the ileum has been unsatisfactory. This is probably due to insufficient attention to details in the study of the small bowel pattern.

The author reports one case in which post irradiation damage to the ileum was proved at operation 32 years after irradiation. The patient, a 64 year old white male, was given roentgen therapy following right orchiectomy and lymph node dissection for teratoma of the testicle. He received three courses of roentgen therapy. The estimated dose to the small bowel was 1,900 r to 2,300 r. Following his treatments the patient had continuing abdominal bloating, with episodes of indigestion up to the time of his admission 32 years later. Initial roentgenograms of the abdomen showed dilated loops of both large and small bowel, suggesting ileus. A small bowel study revealed separation of the barium column with segmentation and loss of the usual mucosal markings. The appearance suggested inflammatory changes such as regional enteritis.

A narrow segment of ileum 5.5 cm. long was resected 40 cm. from the ileocecal valve. The resected segment showed congestion of the peritoneal surface, ulceration of the mucosa and marked congestion of the muscular layer. Microscopic study revealed edema and hyalinization of the submucosa, hypertrophy and fibrosis of the muscularis, and congestion of the serosa. A mucosal ulcer involved over half of the mucosa.—*A. W. Sommer, M.D.*

RADIOISOTOPES

Skillern, Penn G., McCullagh, E. Perry, and Clamen, Marvin. Radioiodine in diagnosis and therapy of hyperthyroidism. *A.M.A. Arch. Int. Med.*, Dec., 1962, *110*, 888–897. (From: Department of Endocrinology and Metabolism, The Cleveland Clinic Foundation, Cleveland, Ohio.)

The authors comment that the term "toxic nodular goiter" implies that the hyperthyroidism is caused by a hyperfunctioning nodule or nodules in the goiter. A study of numerous articles on this subject reveals that a variable number of patients with Graves' disease are usually included in this group. Without the aid of a properly interpreted scintigram, it is sometimes clinically impossible to make the important differentiation of a hyperfunctioning adenoma from Graves' disease with an incidental nonfunctioning adenoma (or adenomas). The scintigram is not infallible if the patient has been taking an antithyroid drug or thyrotropin injections, or if there has been previous surgery.

Diagnostic studies with radioiodine were done on 46 hyperthyroid patients with a hyperfunctioning adenoma ("hot nodule") confirmed by scintigraphy. Twenty-five (54 per cent) patients had normal 24 hour uptakes of less than 50 per cent, and 12 (26 per cent) had between 20–40 per cent uptake. The average 24 hour radioiodine uptake in these 46 patients was 48.6 per cent.

Only one hyperfunctioning adenoma was found in each goiter and no significant uptake was observed in the normal thyroid tissue outside the adenoma. All the adenomas were estimated to be more than 3 cm. in diameter. In all except 2 patients, the predominantly palpable nodule was the hyperfunctioning adenoma.

None of the 46 patients had the ocular signs characteristic of Graves' disease.

Twenty-one of the 46 patients were treated with large initial doses of radioiodine, ranging from 28 to 56 mc (average dose 42.2 mc). Of these 21 patients, 16 were euthyroid within 2 months and all were euthyroid within 4 months after treatment. No clinical exacerbation was noted after therapy, and hypothyroidism did not develop in any of the 21 patients. The hyperfunctioning adenoma did not disappear in any of the patients, but always did decrease in size from 25–75 per cent.

The recommended dose by the authors is 20 mc I^{131} delivered into the adenoma, based on the radioiodine uptake. In previous experience with smaller doses ranging from 10–30 mc, repeat doses were needed in over two-thirds of the patients.

Despite the excellent results using these doses in this condition, the authors still prefer surgical treatment in most patients until the potential risk of using a large dose of radioiodine has been further evaluated. Radioiodine is recommended for the poor operative risk, the elderly patient, and the patient who is eager to avoid, or refuses, surgery.—*John A. Campbell, M.D.*

Kusakabe, Tunesuke, and Miyake, Tadashi. Defective deiodination of I^{131}-labeled L-diiodotyrosine in patients with simple goiter. *J. Clin. Endocrinol. & Metabol.*, Feb., 1963, *23*, 132–139. (From: Department of Internal Medicine, Kyoto University Medical School, Kyoto, Japan.)

The authors have studied a defect involving deiodination of I^{131}-L-diiodotyrosine in a group of 10 patients, all of whom had simple goiters. Of these 10, 4 were members of one family and another 2 were members of a second family. The other 4 individuals came from families with no history of goiter. All patients in the series were euthyroid. Most were noted to have had goiters since infancy or childhood. Detection of the labeled L-diiodotyrosine was accomplished by the method of Stanbury involving chromatography of fractional urine samples. Needle biopsy of thyroid tissue was obtained from 6 of the patients and chromatography was carried out on tissue extracts. It was found that all patients in these groups had defects in peripheral deiodination, but 6 of them, including 4 members of the same family, showed not only peripheral but thyroidal deiodination defects.

Inability to deiodinate iodotyrosines is known to be an an inherited error of metabolism. From an extensive pedigree of one of the families studied, it was concluded that the gene which produces deiodination defects both in the thyroid and in the periphery is an autosomal dominant which shows almost complete penetrance in women.—*Frederick J. Bonte, M.D.*

Gabriel, James B., Solomon, Nathan A., Fierst, Sidney M., and Sass, Martin. Evaluation of chromic oxide marker in absorption of fat. *Am. J. Digest. Dis.*, Mar., 1963, *8*, 280–291. (Address: Dr. Sidney M. Fierst, 835 Ocean Avenue, Brooklyn 26, N. Y.)

A method has been designed exploring the use of inert chromic oxide indicator to determine the completeness of stool collections used for measuring the absorption of I^{131} triolein.

Eleven patients were studied. Fecal collections were begun immediately after the simultaneous administration of radioactive I^{131} triolein and chromic oxide in separate gelatin capsules. The stool collections were continued until a specimen lacking both green chromic oxide and radioactivity was obtained.

Analysis of results indicates that fairly accurate estimation of total fecal excretion of I^{131} triolein might be obtained from partial fecal collections by pooling stools having on inspection high chromic oxide content (green). Since the outcome depends primarily on the relationship between fecal radioactivity and chromic oxide concentrations and not on the absolute recovery of each substance, the need for carefully supervised collections is minimized. This provides a simple, practical substitute for the conventional balance techniques.—*Bernard Loitman, M.D.*

Malinow, Manuel René, Moguilevsky, Jaime A., Lema, Baltasar, and Bur, Grato E. Vascular and extravascular radioactivity after the injection of estradiol $6,7H^3$ in the human being. *J. Clin. Endocrinol. & Metabol.*, Mar., 1963, *23*, 306–310. (From: Institute of Physiology, Buenos Aires Medical School, Buenos Aires, Argentina.)

Because of the recent interest in the role of estrogen compounds in reducing atherosclerosis in cholesterol-fed chickens, the fate of intravenously administered estradiol $6,7H^3$ in humans was studied.

Terminal patients were injected with 250–750 μc of estradiol $6,7H^3$ which had been incorporated into 1 mg. of estradiol 17B. There were no untoward effects evident attributable to the procedure. Complete postmortem examination was carried out immediately and tissues were placed in 4 per cent formaldehyde solution. Tissue slices were prepared with a freezing microtome, mounted in contact with stripping photographic film and left in darkness in the ice box for 5–12 months. Developing was done using the standard photographic technique and the tissues were stained with hematoxylin.

Areas of radioactivity were found in the following distribution in all 4 patients: in normal and atheromatous intima and in the endothelium and adventitia of medium sized coronary arteries. Radioactivity was also found throughout the endothelium of the large vessels in the kidney, spleen, liver, pancreas and lungs. The epithelial lining of glands and organs was likewise the site of deposition of radioactivity.

These studies do not indicate a local biologic action at the sites of deposition of the estrogen. The findings suggest that intravenous injection of microcrystals of estradiol could be an effective method of depositing the hormone and/or its metabolites within the arterial walls.—*David Morse, M.D.*

Chang, M. C., Hunt, Dorothy M., and Harvey, Elmer B. Effects of radiocobalt irradiation of pregnant rabbits on the development of fetuses. *Anat. Rec.*, Mar., 1963, *145*, 455–466. (From: Worcester Foundation for Experimental Biology, Shrewsbury, Mass.)

Female rabbits were artificially inseminated and injected intravenously to induce ovulation. The day of insemination was considered as day zero. The animals were irradiated by a radiocobalt source on various days after insemination. Following irradiation at 400 r, on day 2, 4 and 6 before implantation, 24 per cent of the embryos implanted, and 19.9 per cent developed into apparently normal fetuses. The same amount of irradiation given on day 7 or 8 at the time of implantation or soon after caused death of all the embryos although 61 per cent implanted. Similar irradiation on day 9, 10 or 11 resulted in 16.5 per cent of living fetuses with a high incidence of congenital malformations and irradiation on day 12, 13 and 14 resulted in 35 per cent of living fetuses again with a high incidence of malformations. With irradiation on days 15 to 22, 30 per cent of the embryos developed into living, apparently normal fetuses.

When the irradiation was reduced to 250 r on day 8, it did not cause death of all embryos and when similar irradiation was given on days 8 to 14 there were 51 to 60 per cent living fetuses with a low incidence of abnormalities.

The authors report that the size of fetuses was distinctly reduced following irradiation on days 11 to 16, but not by irradiation administered before or after this period.—*Arthur E. Childe, M.D.*

Dixon, Andrew D., and Hoyte, David A. N. A comparison of autoradiographic and alizarin techniques in the study of bone growth. *Anat. Rec.*, Jan., 1963, *145*, 101–113. (From: Departments of Anatomy, University of Manchester, England and University College of the West Indies, Jamaica.)

The authors compare calcium 47 radioautographs of the growing animal skull with results obtained by an interesting old technique. Alizarin and certain madder derivatives may be used as intravital stains for growing bone. Gross macerated specimens are employed for evaluation of bone growth using the alizarin red stain method.

A number of excellent contact radioautographs of growing bone sections from young rats and rabbits are shown and are compared with photographs of alizarin preparations.

In their discussion the authors point out that alizarin red dye is rapidly absorbed and fixed in bone growth sites with no apparent toxic effect in the form of impairment of subsequent normal bone growth. The whole specimen, for example the skull, is used for gross studies of the sort which cannot be made with radioactive tracer, for the latter requires sectioning for radioautography. It is further pointed out that the disposition of radioactive calcium in growing bone is similar to that obtained from alizarin red specimens and the two methods are regarded as complementary in the investigative study of bone growth.—*Frederick J. Bonte, M.D.*

25 YEARS of integrity have helped us to become America's largest buyers of

USED X-RAY FILM

- We purchase all makes and sizes from any point in the nation, and pay the freight cost.
- We remit in advance if desired, or promptly after receipt and tally of the value.
- Write for prices today. We will send shipping labels, and direct your film to our nearest plant.

DONALD McELROY, INC.

53 W. Jackson Blvd., Chicago 4, Ill.

Subscribe today to

THE JOURNAL OF THE CANADIAN ASSOCIATION OF RADIOLOGISTS

published quarterly: March, June, September and December. It is the **official organ** of **The Canadian Association of Radiologists.**

Price $3.50 per annum in Canadian or equivalent funds.

The Canadian Association of Radiologists,
1555 Summerhill Avenue,
Montreal 25, Quebec, Canada

Please enter my subscription to the JOURNAL OF THE CANADIAN ASSOCIATION OF RADIOLOGISTS, for which my cheque is enclosed.

Name ....
(Please print)

Address ....
(Please print)

City .... Province or State .... Country ....

YOU CAN ACQUIRE VALUABLE BACK VOLUMES AND SINGLE ISSUES OF THE PUBLICATIONS OF

The American Roentgen Ray Society

A limited quantity of the issues available are listed below. Orders are subject to the exhaustion of available stock. This offer is subject to withdrawal without notice. **NOTE: For your convenience, the same price—$1.50 per copy—applies to all issues—no quantity discount.**

Order BACK ISSUES of the Journal from:

CHARLES C THOMAS • PUBLISHER 301-327 East Lawrence Avenue **SPRINGFIELD • ILLINOIS**

The American Journal of Roentgenology: 1914-1922

Vol. 1, Nos. May, July, October (1914)
Vol. 2, Nos. April, Nov.-Dec. (one issue) (1915)
Vol. 3, Nos. February thru December (1916)
Vol. 4, Nos. January, April, May, June, Sept., Nov., Dec. (1917)
Vol. 5, Nos. January thru December (1918)
Vol. 6, Nos. January thru August, October thru December (1919)
Vol. 7, Nos. January thru December (1920)
Vol. 8, Nos. January thru December (1921)
Vol. 9, Nos. January thru December (1922)

The American Journal of Roentgenology and Radium Therapy: 1923-1929

Vol. 10, Nos. January thru December (1923)
Vol. 11, Nos. January thru June (1924)
Vol. 12, Nos. July thru December (1924)
Vol. 13, Nos. January thru June (1925)
Vol. 14, Nos. July thru December (1925)
Vol. 15, Nos. January thru June (1926)
Vol. 16, Nos. July thru December (1926)
Vol. 17, Nos. January thru June (1927)
Vol. 18, Nos. July thru December (1927)
Vol. 19, Nos. January thru June (1928)
Vol. 20, Nos. July thru December (1928)
Vol. 21, Nos. January thru June (1929)
Vol. 22, Nos. July thru December (1929)

The American Journal of Roentgenology and Radium Therapy: 1930-1951

Vol. 23, Nos. 1, 2, 3, and 6 (1930)
Vol. 24, Nos. 1-6 (July-Dec. 1930)
Vol. 25, Nos. 1-6 (Jan.-June 1931)
Vol. 26, Nos. 1-6 (July-Dec. 1931)
Vol. 27, Nos. 1-6 (Jan.-June 1932)
Vol. 28, Nos. 1-6 (July-Dec. 1932)
Vol. 29, Nos. 1-6 (Jan.-June 1933)
Vol. 30, Nos. 1-6 (July-Dec. 1933)
Vol. 31, Nos. 1-6 (Jan.-June 1934)
Vol. 32, Nos. 1-6 (July-Dec. 1934)
Vol. 33, Nos. 1-6 (Jan.-June 1935)
Vol. 34, Nos. 1-6 (July-Dec. 1935)
Vol. 35, Nos. 1-6 (Jan.-June 1936)
Vol. 36, Nos. 1-6 (July-Dec. 1936)
Vol. 37, Nos. 1-6 (Jan.-June 1937)
Vol. 38, Nos. 1-3 (July-Sept. 1937)
Vol. 39, Nos. 1-6 (Jan.-June 1938)
Vol. 40, Nos. 2-6 (Aug.-Dec. 1938)
Vol. 41, Nos. 1-6 (Jan.-June 1939)
Vol. 42, Nos. 2-6 (Aug.-Dec. 1939)
Vol. 43, Nos. 2-6 (Feb.-June 1940)
Vol. 44, Nos. 1-6 (July-Dec. 1940)
Vol. 45, Nos. 3 (March 1941)
Vol. 46, Nos. 6 (December 1941)
Vol. 47, Nos. 1-6 (Jan.-June 1942)
Vol. 48, Nos. 1-6 (July-Dec. 1942)
Vol. 49, Nos. 2-6 (Feb.-June 1943)
Vol. 51, Nos. 5-6 (May-June 1944)
Vol. 52, Nos. 2 (August 1944)
Vol. 54, Nos. 2-6 (Aug.-Dec. 1945)
Vol. 55, Nos. 5-6 (May-June 1946)
Vol. 56, Nos. 1-6 (July-Dec. 1946)
Vol. 57, Nos. 3-6 (March-June 1947)
Vol. 58, Nos. 1-6 (July-Dec. 1947)
Vol. 59, Nos. 2-6 (Feb.-June 1948)
Vol. 60, Nos. 1-6 (July-Dec. 1948)
Vol. 61, Nos. 3 (March 1949)
Vol. 62, Nos. 2, 4, 5, 6 (Aug. Oct. Nov. Dec. 1949)
Vol. 63, Nos. 1 (January 1950)
Vol. 64, Nos. 1-6 (July-Dec. 1950)
Vol. 65, Nos. 1, 2, 4, 5, 6 (1951)
Vol. 66, Nos. 1-6 (July-Dec. 1951)

The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine: 1952-1962

Vol. 67, Nos. 1, 3, 4, 5, 6 (1952)
Vol. 68, Nos. 1-6 Inclusive (July-Dec. 1952)
Vol. 69, Nos. 1, 2, 3, 4, 6 (1953)
Vol. 70, Nos. 1-6 Inclusive (July-Dec. 1953)
Vol. 71, Nos. 1-6 Inclusive (Jan.-June 1954)
Vol. 72, Nos. 1-6 Inclusive (July-Dec. 1954)
Vol. 73, Nos. 1-6 Inclusive (Jan.-June 1955)
Vol. 74, Nos. 1-6 Inclusive (July-Dec. 1955)
Vol. 75, Nos. 1-6 Inclusive (Jan.-June 1956)
Vol. 76, Nos. 1-6 Inclusive (July-Dec. 1956)
Vol. 77, Nos. 1-6 Inclusive (Jan.-June 1957)
Vol. 78, Nos. 1-6 Inclusive (July-Dec. 1957)
Vol. 79, Nos. 1-6 Inclusive (Jan.-June 1958)
Vol. 80, Nos. 1-6 Inclusive (July-Dec. 1958)
Vol. 81, Nos. 1-6 Inclusive (Jan.-June 1959)
Vol. 82, Nos. 1-6 Inclusive (July-Dec. 1959)
Vol. 83, Nos. 1-6 Inclusive (Jan.-June 1960)
Vol. 84, Nos. 1-6 Inclusive (July-Dec. 1960)
Vol. 85, Nos. 1-6 Inclusive (Jan.-June 1961)
Vol. 86, Nos. 1-6 Inclusive (July-Dec. 1961)
Vol. 87, Nos. 1-6 Inclusive (Jan.-June 1962)
Vol. 88, Nos. 1-6 Inclusive (July-Dec. 1962)
Vol. 89, Nos. 1-6 Inclusive (Jan.-June 1963)

BRITISH JOURNAL OF RADIOLOGY

SUPPLEMENT No. 9

THE SPECTRA OF X RAYS SCATTERED IN LOW ATOMIC NUMBER MATERIALS

By W. R. Bruce, M.D., Ph.D., and H. E. Johns, Ph.D., F.R.S.C.

The complicated effects of multiple scattering have always presented a major difficulty to analysts of X-ray beams traversing matter. In this Supplement the authors describe how the Monte Carlo method of computation may be used to allow for multiple scattering when studying the penetration of X-ray beams. A full discussion of their combination of analytical and Monte Carlo methods is presented and much information on the spectra of X-ray beams in the photon energy range from 50 to 1250 ke V is provided in the form of graphs and tables, with the main emphasis on data for beams traversing water. This Supplement will interest all those concerned with the use of X rays in radiotherapy and in radiobiological studies.

Price: 12*s*. 6*d*. $2.00 (One copy is allowed to each member at 7/6*d*—*U.S.A.* $1.50)

SUPPLEMENT No. 10

DEPTH DOSE TABLES FOR USE IN RADIOTHERAPY

(containing 77 tables, three full-page and two half-page graphs)

The value of central axis depth dose and related data in radiotherapy was evident from the heavy demand made for *Supplement No. 5* (1953), "Central Axis Depth Dose Data". When stocks of the latter were exhausted three years ago, it was decided to revise the original data in the light of more recent experimental work, and to extend the coverage to the higher energies now coming into general use. This task was undertaken by the Scientific Subcommittee of the Hospital Physicists' Association.

The new edition contains nine main sections covering electromagnetic radiations ranging from Grenz rays (H.V.T. 0.01 mm of Al) up to 31 MV betatron X-rays, and including electron beams (2 to 30 MeV). Every effort has been made to ensure that tables are adequately explained as to origin, possible sources of error and limitations of applicability. Where significant differences from the earlier data occur, they are discussed by the individual reviewers of the sections concerned.

This Supplement provides the most comprehensive selection of central axis data in existence, and has been compiled by acknowledged experts in the field.

Price: 45*s*. $7.50 (One copy is allowed to each member at 32/6*d*—*U.S.A.* $6.50)

obtainable from

THE BRITISH INSTITUTE OF RADIOLOGY
32 WELBECK STREET, LONDON, W.1
and from leading booksellers all over the world

INDEX TO ADVERTISERS

Ansco (General Aniline & Film Corp.) .... xvi, xvii
Atomic Energy of Canada Ltd. xxxi

Barnes-Hind Barium Products .... xii, xiii
Bell-Craig, Inc. xxx
British Institute of Radiology xlvii
Buck X-Ograph Company xxviii

Canadian Association of Radiologists xlv

Dick X-Ray Company xliii
du Pont, E. I. de Nemours Co. .... ix, x

Eastman Kodak Company .... xxxv, xxxix, xl

Fougera, E. & Company, Inc. xxxiii

General Electric Company .... xxiii, xxv, xxvii, xxix

Halsey X-Ray Products .... vi, xlix
High Voltage Engineering Corp. i
Hunt, Philip A., Company xxvi

Ilford, Inc. xx

Karger, S. xliv
Keleket X-Ray Corp. xxi

Liebel-Flarsheim Company (Div'n. of Ritter Company) xviii
Low X-Ray Corporation xix

Mallinckrodt Chemical Works .... xiv, xv
McElroy, Donald, Inc. xlv
Minnesota Mining & Manufacturing Corp. .... xxxvi, xxxvii

Philips, N. V., Gl. xxiv
Picker X-Ray Corporation .... xi, xliii, Fourth cover
Profexray, Inc. .... Third cover

Schick X-Ray Company xxxii
Siemens America, Inc. xxii
Squibb, E. R., & Sons v
Standard X-Ray Company xli

Thomas, Charles C, Publisher .... xxxviii, xlii

Walker Industries viii
Westinghouse Electric Corporation .... Second cover
Winthrop Laboratories .... vii, xxxiv
Wolf X-Ray Products l

●

We try to present an accurate index. Occasionally this may not be possible because of a last-minute change or an omission.

No matter how you look at it —

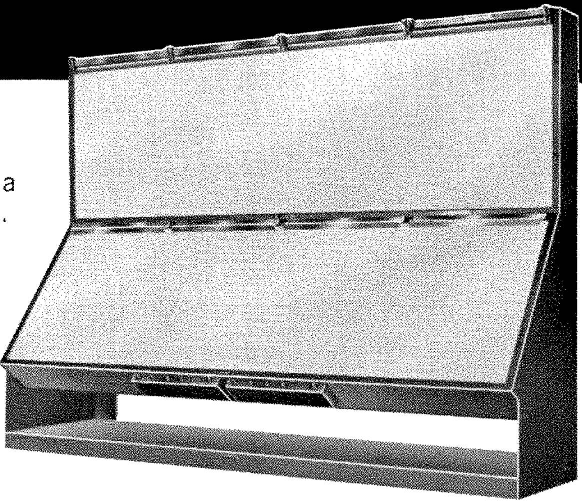
x-ray viewing is less of a strain with

HALSEY EASY-VIEW BANKS

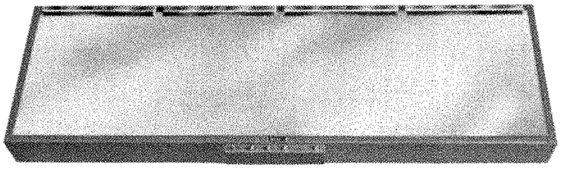
Standing or sitting, you'll find the viewing more comfortable — and diagnostic comparison of a series far easier — with these new angulated banks.

Available in wall-mounted and mobile models (extra accessories: shelf; shelf drawer; central switch panel instead of individual switches on each illuminator tier).

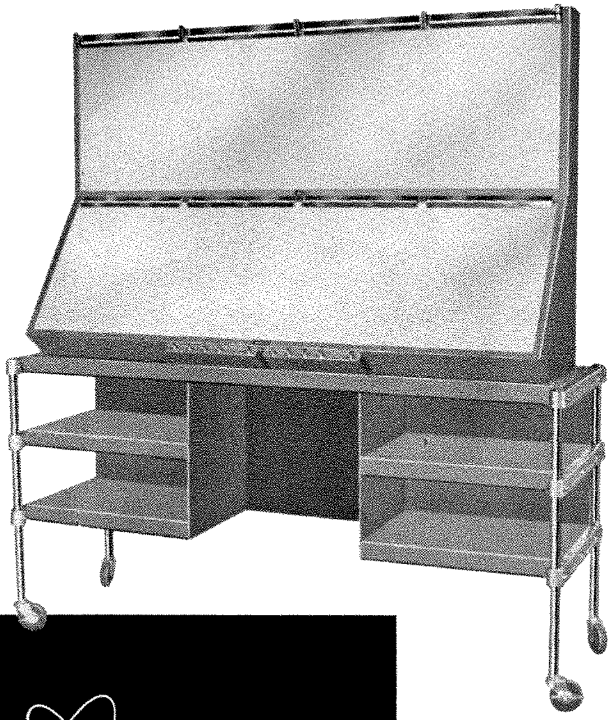
Supplied with Instant Grip continuous film holder — grips film instantly, releases as readily, automatically provides just the right holding pressure; grips any size film, anywhere along the viewing surface. Wet-film holders included on vertical sections.



No. 2308-I-A-SH-CS
4-on-4, with shelf and
central switch panel



No. 2304-I-A-CS
4-bank, with central
switch panel



ALL HALSEY ILLUMINATORS FEATURE . . .

- Photometer-tested lighting to insure even light distribution
- Improved P-80 Plexiglas front panel — ground glass finish on its inner surface provides 10% better lighting
- "Invisible" welds — with no sharp corners
- Easily removable Plexiglas panel to prevent chipping of corners
- Grommeted electric cord set with molded rubber plug to protect electrical connections against damage due to accidental tugs
- UL approval

No. 2308-I-MD-A-CS
4-on-4, with mobile desk base
and central switch panel
4-bank model also available

Through your dealer — or write for detailed literature

HALSEY

HALSEY X-RAY PRODUCTS, INC.
1425-37th Street, Brooklyn 18, N.Y.

CHICAGO: 7321 Monticello Ave., Skokie, Illinois
LOS ANGELES: 1816 W. 8th St., Los Angeles 57, Calif.

In your circle, you'll never find a protective companion which wears with greater comfort than Superflex. Like an old friend, Wolf's Superflex glove is comfortable, easy-to-live-with, and can always be relied on . . . Like an old friend, Superflex gloves have many faces to their personality, and if the standard sizes and styles do not quite accommodate to your needs, why, just ask—we'll be pleased to craft to your exact measurements.

Your dealer will be happy to show you the broad selection of Superflex friends available — or — better — why not drop us a card for a **complete** Wolf catalog?

With a Wolf Superflex glove
YOU'LL HAVE THE SITUATION WELL IN HAND.

WOLF X-RAY PRODUCTS INC.

Main Office: 93 Underhill Avenue, Brooklyn 38, New York
Western Service Center (Serving Areas West of Denver)
1909 W. 9th Street, Los Angeles 6, California

FOUNDED IN 1906 AS THE AMERICAN QUARTERLY OF ROENTGENOLOGY

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

CALCU
CENTRA
LIBRA
UNIVERS

OFFICIAL ORGAN OF
THE AMERICAN ROENTGEN RAY SOCIETY
THE AMERICAN RADIUM SOCIETY

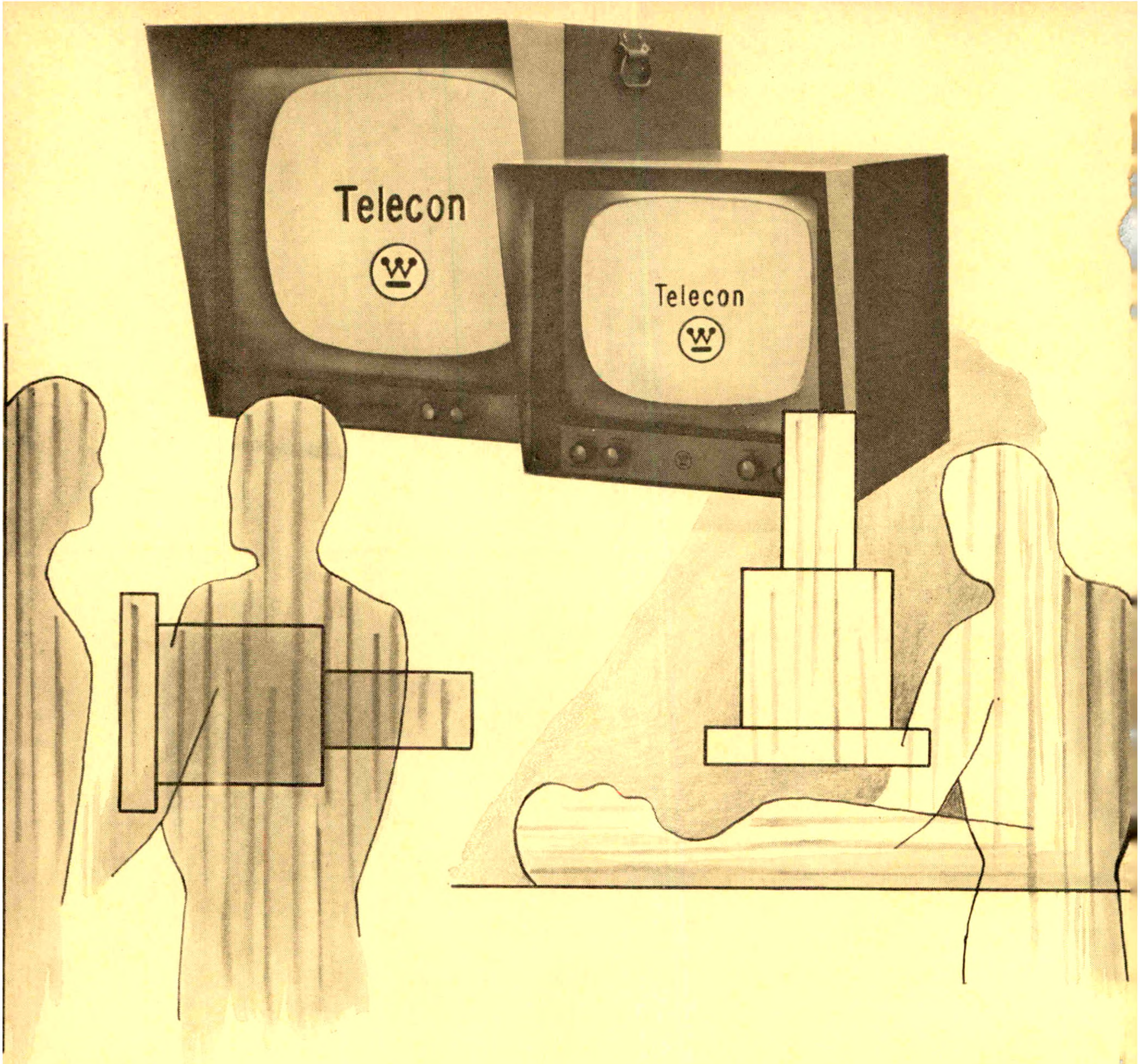
TRAIAN LEUCUTIA, Editor
KENNETH L. KRABBENHOFT, Assistant to the Editor

ASSOCIATE EDITORS
HARRY HAUSER RUSSELL H. MORGAN EDWARD B. D. NEUHAUSER
WENDELL G. SCOTT

CONSULTING EDITORIAL BOARD
PAUL C. AEBERSOLD
OSCAR V. BATSON
JOHN CAFFEY
ROSS GOLDEN
PAUL C. HODGES
HOWARD B. HUNT
JOHN H. LAWRENCE
REED M. NESBIT
EUGENE P. PENDERGRASS
U. V. PORTMANN
LAURISTON S. TAYLOR
OWEN H. WANGENSTEEN
SHIELDS WARREN

Issued Monthly for the American Roentgen Ray Society by
CHARLES C THOMAS · PUBLISHER · SPRINGFIELD · ILLINOIS

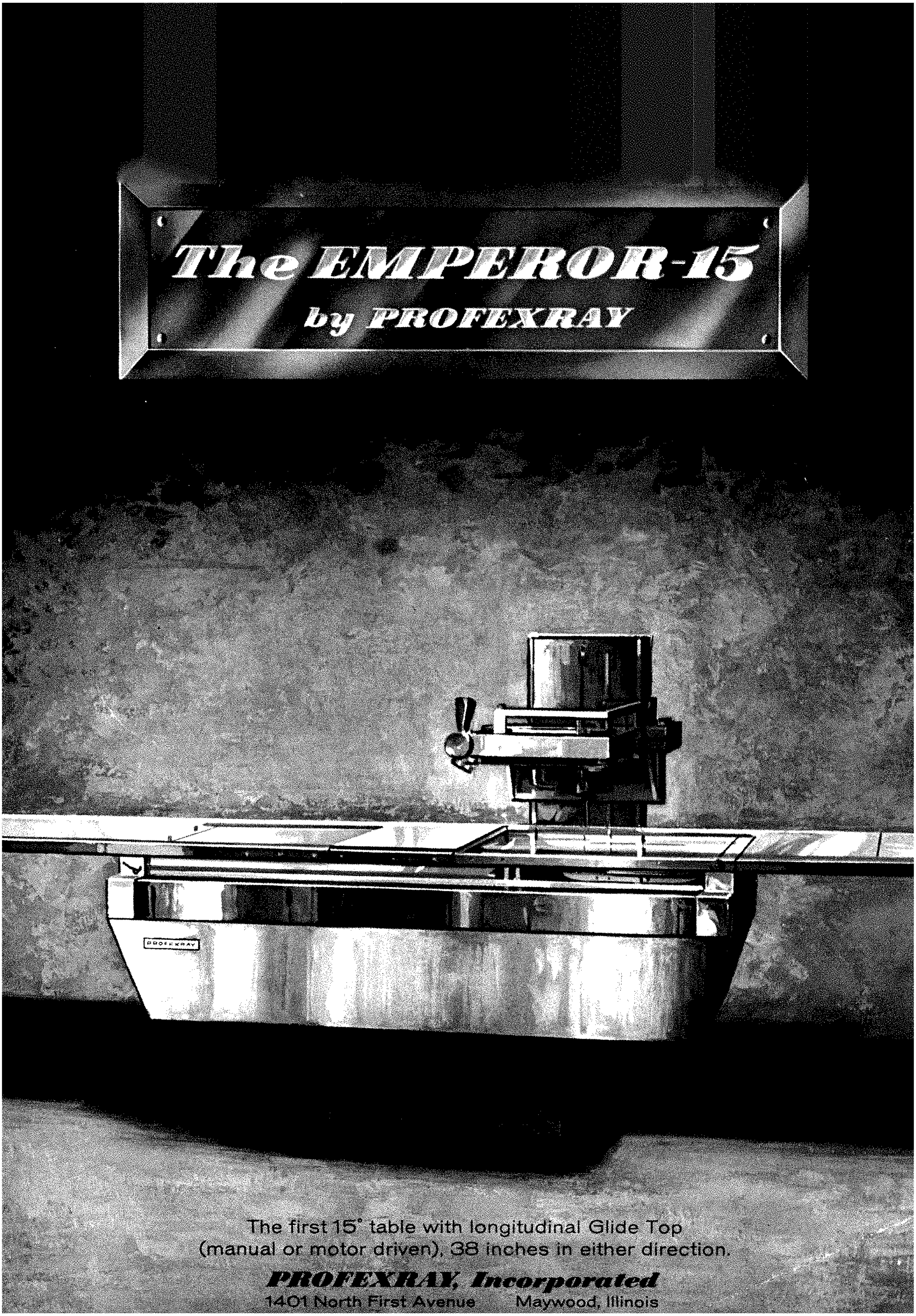
VOLUME 90 DECEMBER, 1963 NUMBER 6
INDEX NUMBER



Now, TV Fluoroscopy convenience at the cost of mirror viewin

TELECON—Specifically designed for daily routine fluoroscopy. This new concept of fluoroscopy consists of a high gain (6 or 7 inch) image intensifier with a high-quality vidicon camera coupled direct to the output phosphor. Fluoroscope with TV convenience in a lighted room. Saves time, no dark adaptation required. TV monitors 8, 14, 17, 21, 24, and 27 inch sizes can be used in any number of locations. Kinescope or videotape recording ca easily be added. Routine spotfilm radiographs are done wit the famous side-loading Nassau spotfilm device. Here, for th first time, is a new low-cost TV fluoroscopy system. Quality co trolled reliability you can depend on. Write for brochure. Wes inghouse Electric Corp., 2519 Wilkens Ave., Baltimore, Md. 2120

We never forget how much you rely on Westinghouse



The first 15° table with longitudinal Glide Top
(manual or motor driven), 38 inches in either direction.

PROFEXRAY, *Incorporated*
1401 North First Avenue   Maywood, Illinois

GENERAL INFORMATION

Manuscripts offered for publication and other correspondence relating to the editorial management and books for review should be sent to Dr. Traian Leucutia, Editor, 110 Professional Building, Detroit 1, Michigan. Contributions may be sent in foreign languages and will be translated if found acceptable. Original articles are published with the understanding that they are contributed exclusively to THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE.

A certain number of illustrations will be supplied free of cost; but special arrangements must be made with the Editor and Publisher for excess illustrations and elaborate tables.

Fifty reprints are furnished without charge to authors. Additional reprints may be purchased according to a scale of prices that accompanies galley proofs. As soon as each issue is printed, the type is destroyed except for reprint orders *in hand.* Reprint orders *must* be returned with corrected galley proof to the Editorial Office if additional reprints are desired.

Correspondence regarding subscriptions, advertisements, and other business relating to THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE should be addressed to Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois. (All requests to be submitted in writing.)

Manuscripts should be typewritten, with double spacing, and good margins (not on thin paper) and the *original* should be sent to the Editor. The author should keep a carbon copy, as the original is not returned. The name of the author should appear on each sheet of manuscript. Tabular materials should be typed on separate sheets; likewise bibiliographical lists, footnotes, etc.

Drawings and charts for reproduction should be made in black (*never* in blue). Photographic prints of plates or slides on glossy paper produce the best half-tones.

All photographs and drawings intended for illustrations should be numbered, the top plainly indicated, and an abbreviated title of the paper placed on the back of *each one*.

Legends for illustrations should be typewritten in a single list, double spaced, with numbers corresponding to those on the photographs and drawings, instead of attaching each legend to its corresponding figure.

Care in preparation of bibliographies will save much time and correspondence. Each reference in a bibliography should include the following information in order the indicated: Name of the author with initials; title of the article; name of the periodical year, volume and pages. It is requested that the authors use the following as model:

1. Olcott, C. T., and Dooley, S. W. Agenesis of lung of infant. *Am. J. Dis. Child.*, 1943, *65*, 766–780.

The month should be given if the reference is to an issue of the current year. An alphabetical arrangement of the authors is requested.

The author should always place his full address somewhere on his manuscript. This is very important and is often omitted.

For information regarding membership in the American Roentgen Ray Society, address the Chairman of the Executive Council, Dr. J. P. Medelman, 110 Birchwood Avenue, White Bear Lake 10, Minnesota.

For information regarding the program of the annual meeting of the American Roentgen Ray Society, address the President-Elect, Dr. Harold O. Peterson, 1995 West County Road "B," St. Paul 13, Minnesota.

For information regarding membership in the American Radium Society, address the Secretary, Dr. Justin J. Stein U.C.L.A. Medical Center, Los Angeles 24, California.

For information regarding the program of the annual meeting of the American Radium Society, address the President, Dr. Charles G. Stetson, 97 Lawrence Parkway, Tenafly, New Jersey.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE is owned maintained by, and in the interests of, the American Roentgen Ray Society, Inc. It is issued monthly by Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois. THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE does not hold itself responsible for any statements made or opinions expressed by any contributors in any article published in its columns.

Delivery is not guaranteed. Replacements are not guaranteed nor promised, but will be attempted if extra single copies are available and only if requested within 30 days from first of month following publication (17th of month) for domestic subscribers and 60 days for foreign subscribers.

Annual subscription price is as follows: United States, U. S. Possessions, U. S. Trusteeships, Pan-American Union, and Canada, $15.00; other countries $17.00. Prices for back volumes quoted on application. Extra single copies of back issues, if available, $1.50, postpaid. Current subscriptions may begin with any issue. Remittance should be sent to CHARLES C THOMAS, PUBLISHER, 301–327 East Lawrence Avenue, Springfield, Illinois, U.S.A.

ADDRESS CHANGE—When a change of address is necessary please allow at least 60 days notice and preferably 90 days. When ordering a change of address, send the Publisher both the old and new address.

Entered as Second-class at Springfield, Illinois under the
Act of March 3, 1879. Printed in U.S.A.

Second-class postage paid at Springfield, Illinois
and at additional mailing offices.

Copyright © 1963, by AMERICAN ROENTGEN RAY SOCIETY, Inc. No part may be duplicated or reproduced without permission of the Publisher.

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 90 DECEMBER, 1963 No. 6

CONTENTS

On the Preservation of an Image; The President's Address. RALPH M. CAULK, M.D. 1121
Some New Portable Radioactive Sources for Diagnostic Radiography. KENNETH L. KRABBENHOFT, M.D., AND FARNO L. GREEN, M.S. . . . 1123
Normal and Pathologic Roentgen Anatomy of the Middle Ear and Mastoid Process. LEWIS E. ETTER, M.D., AND LAWRENCE C. CROSS, R.T. . 1143
Technique for the Study of the Middle Ear; With Special Reference to Cholesteatoma. ANDRÉ SANSREGRET, M.D. 1156
Pituitary Insufficiency Following Meningitis; Report of a Case with Roentgenographic Signs Simulating Osteoporosis Circumscripta. DONALD G. WETHERBEE, M.D., AND JOHN W. TURNER, M.D. 1167
Traumatic Pneumocephalus. ROBERT J. KAHN, M.D., AND ALVIN L. DAYWITT, M.D. 1171
The Ventricular Span in Cerebral Pneumography. H. JOACHIM BURHENNE, M.D., AND HUGH DAVIES, D.M. 1176
Tuberculoma of the Brain. LEONARD BERLIN, M.D. 1185
Diencephalic Pseudotumor Effect. LEON LOVE, M.D., SANFORD J. LARSON, M.D., AND BEAUVOIR EDMOND, M.D. 1193
Pantopaque Anterior Basal Cisternography of the Posterior Fossa. HARVEY GASS, M.D. 1197
Convenient Pneumoencephalography. A. D. SEARS, M.D. 1205
Cervical Diskography; A Help or Hindrance in Evaluating Neck, Shoulder, Arm Pain? RALPH R. MEYER, M.D. 1208
Lateral Intrathoracic Meningocele; Case Report with Preoperative Diagnosis. ARTHUR CHANDLER, M.D., AND EUGENE E. HERZBERGER, M.D. . 1216
Late Spinal Blocks after Tuberculous Meningitis. KAZIMIERZ KOZLOWSKI, M.D. 1220

(*Continued on p. iv*)

Spinal Extradural Cysts; With Report of an Ossified Spinal Extradural Cyst. David J. Rosenblum, M.D., and Joshua R. Derow, M.D. . . . 1227

Displacement of the Linear Thoracic Paraspinal Shadow of Brailsford; An Early Sign in Osteomyelitis of the Thoracic Spine. D. Glyn Millard, M.B., B.S. . . . 1231

Vertebral Epiphysitis: A Comparison of the Clinical and Roentgenologic Findings. Hugh J. Williams, M.D., and David G. Pugh, M.D. . . . 1236

The Roentgenographic Aspects of Pseudogout (Articular Chondrocalcinosis); An Analysis of 20 Cases. Daniel J. McCarty, Jr., M.D., and Marvin E. Haskin, M.D. . . . 1248

Stress Fracture with Spondylolysis. Lee A. Hadley, M.D. . . . 1258

Lumbosacral Retrodisplacement. Theodore A. Willis, M.D. . . . 1263

The Brim Sign; A New Sign Found in Paget's Disease (Osteitis Deformans) of the Pelvis. Thomas R. Marshall, M.D., and J. T. Ling, M.D. . . . 1267

Paget's Disease Confined to One Lumbar Vertebra. Melvyn H. Schreiber, M.D., and Gene A. Richardson, M.D. . . . 1271

Fracture of the Lateral Process of the Talus. Christian V. Cimmino, M.D. 1277

Clinical Evaluation of Conray for Angiography in Patients with Cerebrovascular Disease. Jorge Weibel, M.D., William S. Fields, M.D., E. Stanley Crawford, M.D., Michael E. DeBakey, M.D., and Arthur C. Beall, Jr., M.D. . . . 1281

Sodium Iothalamate, Angio-Conray, in Selective Angiography; Further Evidence of Low Toxicity. J. Gerard Mudd, M.D., and Vallee L. Willman, M.D. . . . 1287

An X-Ray Television Image Storage Apparatus. George Berci, M.D., and Albert J. Seyler, M.E.E., S.M.I.R.E. . . . 1290

Officers . . . 1301

Editorials

The Sixty-fourth Annual Meeting of the American Roentgen Ray Society. Kenneth L. Krabbenhoft, M.D. . . . 1302

Sherwood Moore, M.D., 1880–1963. Wendell G. Scott, M.D. . . . 1305

A. Stanley Kirkland, M.D., 1890–1963. Norman S. Skinner, M.D. . . . 1309

Harry W. Dachtler—Last Charter Member of the American Roentgen Ray Society. John L. Stifel, M.D. . . . 1310

The Scientific Exhibits . . . 1312

The Technical Exhibits . . . 1323

News Items . . . 1325

Book Reviews . . . 1326

Books Received . . . 1327

Abstracts of Radiological Literature . . . 1328

Subject Index to Volume 90 . . . 1337

Author Index to Volume 90 . . . 1347

radiopaque materials . . ."[1]

ANGIOCARDIOGRAPHY with

ANGIO-CONRAY®

[Sodium Iothalamate 80%]

Outstanding safety, ready solubility, superior diagnostic quality

these are some of the qualities that make Angio-CONRAY [sodium iothalamate 80%] the agent of choice for angiocardiography and aortography.

Experimental studies showed Angio-CONRAY [sodium iothalamate 80%] " . . . is less toxic than any of the currently available concentrated angiographic contrast media."[7] Under the most adverse experimental conditions designed for intentional production of renal and spinal cord damage " . . . no evidence of spinal cord or renal injury was noted."[8]

Compared to other available media " . . . the margin of safety in intravenous injections was far greater with Angio-CONRAY [sodium iothalamate 80%]."[9] "There was no vomiting among the dogs receiving 80 per cent sodium iothalamate . . . hematologic determination, biochemical studies, urinalysis and . . . pathologic evaluations were essentially normal . . ."[1]

"Clinically, sodium iothalamate 80% has proved superior for all uses involving intravascular injection of concentrated contrast media."[10]

"Intravenous injections, thoracic aorta injections and intracardiac injections have occasioned absolutely nothing more than transient warmth of only moderate degree."[10] "Low viscosity and ready solubility of Angio-CONRAY [sodium iothalamate 80%] permit ease and speed of injection."[11]

"The diagnostic quality of the angiograms has been excellent . . . particularly . . . in four areas: angiocardiography, intravenous aortography, translumbar aortography, and retrograde catheter thoracic aortography. In each of these examinations, Angio-CONRAY [sodium iothalamate 80%] yielded far superior results."[9]

Each ml. contains 0.8 Gm. sodium iothalamate, not more than 0.135 mg. calcium disodium ethylenediaminetetraacetate as a stabilizer, not more than 0.15 mg. sodium biphosphate as a buffer, and 480 mg. iodine (48%).

Contraindications: For both media, caution is required in cases involving severe systemic disease. In patients with advanced renal disease, use with caution and then only when need for examination dictates. In patients with a history of allergy or those exhibiting a positive reaction to the sensitivity test, facilities and drugs for emergency use must be readily available.

1. Marshall, T. R., and Ling, J. T.: Am. J. Roentgenol. *89*:423 (Feb.) 1963. 2. Smolik, E. A., and Nash, F. P.: Missouri Med. *59*:863 (Sept.) 1962. 3. Hinck, V. C., and Dotter, C. T.: J. Neurosurg. *19*:312 (April) 1962. 4. Steinberg, I., and Evans, J. A.: Radiology *79*:395 (Sept.) 1962. 5. Dotter, C. T., *et al.*: Northwest Med. *61*:41 (Jan.) 1962. 6. Straube, K. R., and Dotter, C. T.: Scientific Paper, 11th Internat. Cong. European Soc. Cardiovascular Surg., Stockholm, Sweden, July, 1962. 7. Sessions, R. T., *et al.*: Surg. Gynec. & Obst. *115*:187 (Aug.) 1962. 8. Bernstein, E. F., *et al.*: Surgery *51*:663 (May) 1962. 9. Foster, J. H., *et al.*: Scientific Exhibit, 111th Annual Meeting A.M.A., Chicago, Illinois, June, 1962. 10. Foster, J. H., *et al.*: JAMA *182*:1009 (Dec. 8) 1962. 11. Kanick, V., and Finby, N.: Radiol. *80*:438 (March) 1963.

Mallinckrodt
® Pharmaceuticals
LINKING CHEMISTRY TO MEDICINE

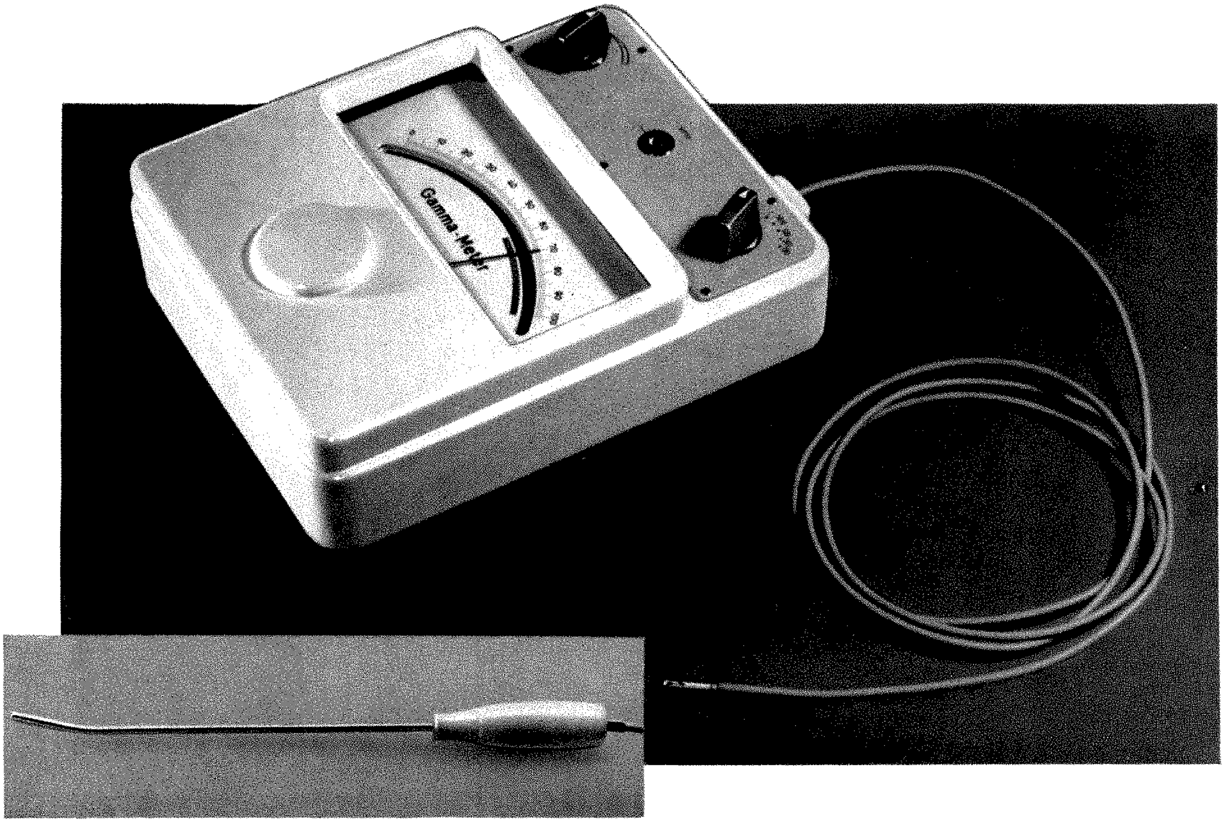
Mallinckrodt®

Mallinckrodt Chemical Works
St. Louis 47, Mo.

SIEMENS

GAMMAMETER

the handy measuring instrument with crystal probe
for radium and radio-cobalt therapy



2 PROBES ARE AVAILABLE:

flexible probe for measurements free in air or in a phantom, and inflexible probe, preferably for intracavitary measurements.

Diameter of both probes $^{1}/_{5}$ inch only.

Punctiform measurement even in extremely inhomogeneous radiation fields of small radioactive preparations, such as radium tubes and cobalt beads.

Convenient introduction and accurate, intracavitary positioning of the graduated, inflexible 10-inch probe.

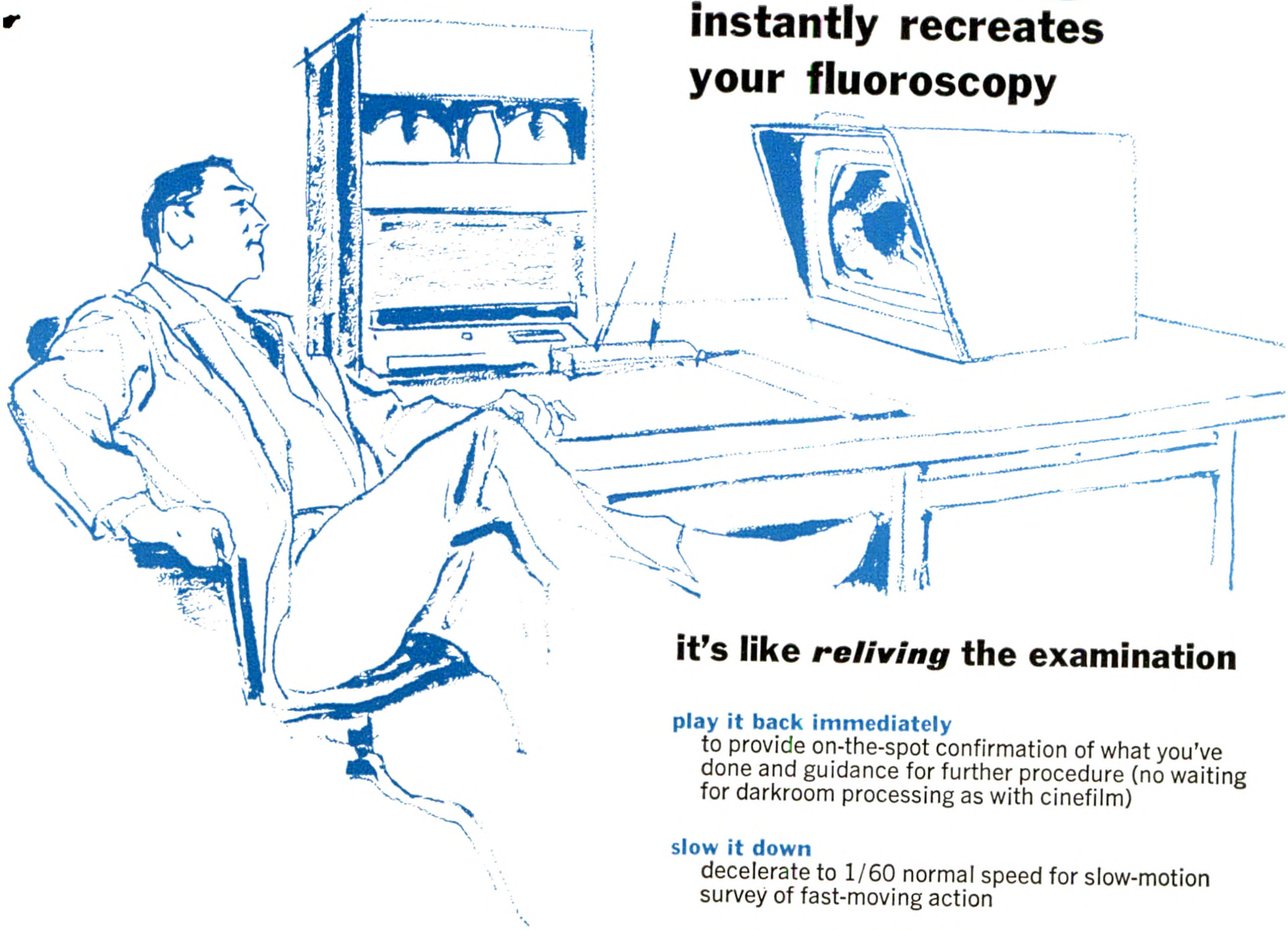
5 measuring ranges: up to 50 r/h, 100 r/h, 200 r/h, 500 r/h, and 1000 r/h.

Independent of electric power. Easily transportable.

SIEMENS MEDICAL OF AMERICA, INC., 685 LIBERTY AVENUE, UNION, N.J.

VideoRecording

instantly recreates your fluoroscopy



it's like *reliving* the examination

play it back immediately
to provide on-the-spot confirmation of what you've done and guidance for further procedure (no waiting for darkroom processing as with cinefilm)

slow it down
decelerate to 1/60 normal speed for slow-motion survey of fast-moving action

"freeze" a decisive moment
stop any significant frame for detailed scrutiny: hold it still for as long as five minutes

study and restudy anytime, now or later
recreate the examination as often as necessary without further irradiating the patient

transmit to multiple monitors
in the room itself, in the radiologist's office, in the auditorium — during the examination or any time later

easy to record
pushbutton start and stop: by remote control at tableside or directly at recorder

The SONY X-Ray Videocorder

. . . is the **only** VideoRecorder on the market which offers the added advantages of **slow-motion** and **single-framing**

. . . is instantly adaptable to any existing TV equipment

. . . is marketed/serviced in the U.S.A. exclusively by Picker

get the full story from your local Picker representative, or write PICKER X-RAY CORPORATION, White Plains, N.Y.

Picker
x-ray

fluoricon

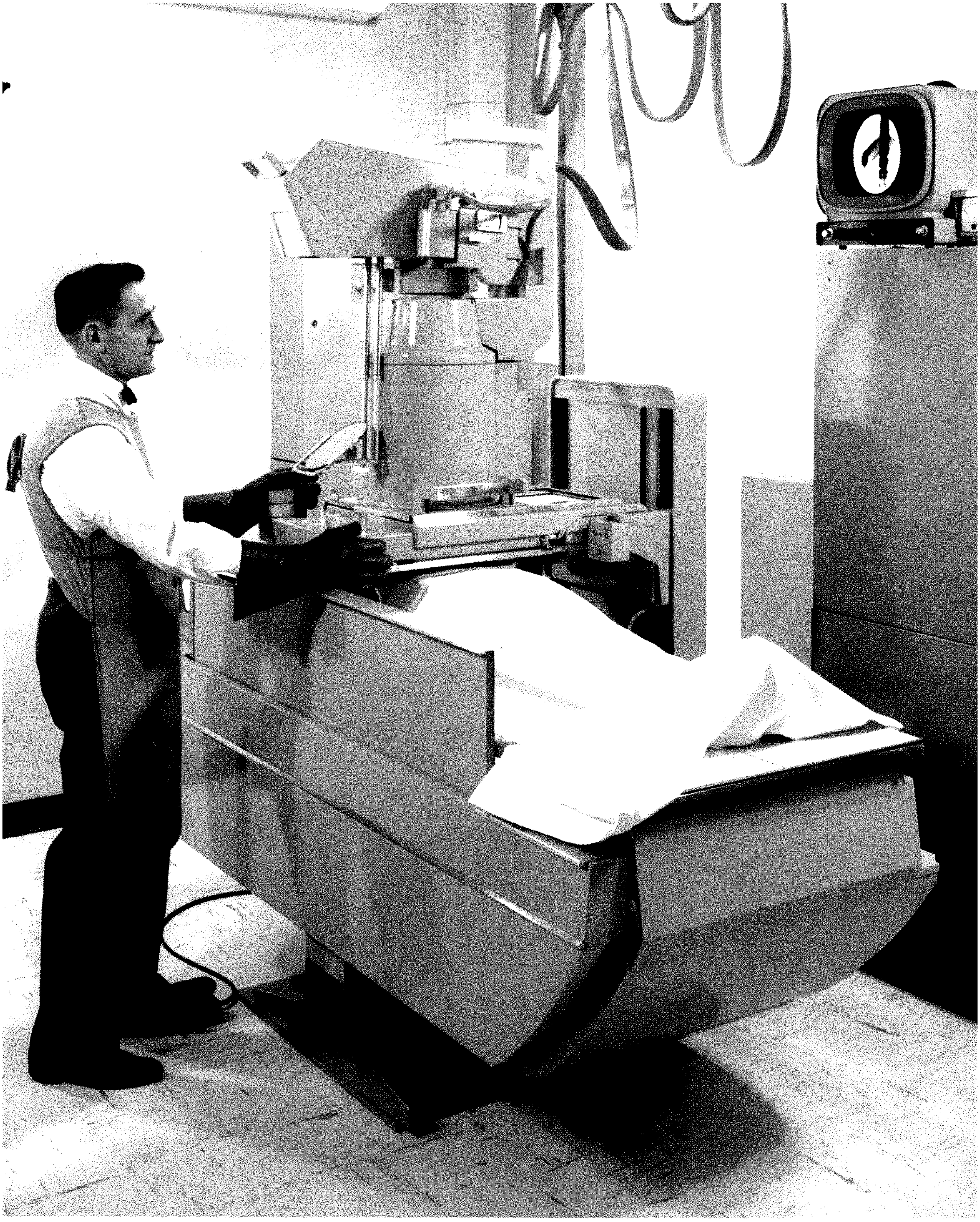
the image of professional versatility

Image intensification reaches new levels of usefulness in FLUORICON. And the key to this superiority is the optical system — described by many radiologists as "the finest optical system in existence today."

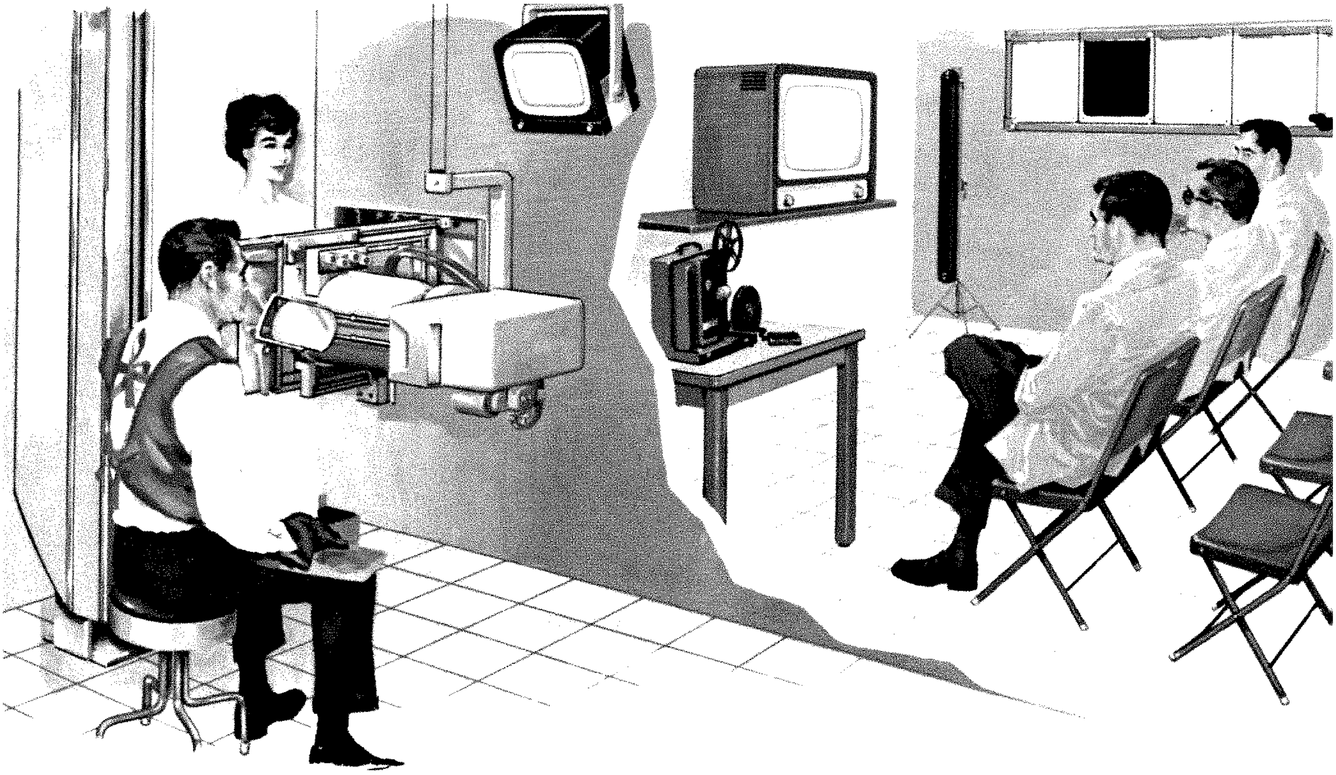
What kind of performance can you expect from FLUORICON? Direct viewing, in normal room light, with a brightness gain of some 3000. Remote viewing with television having an amazing light sensitivity. Simultaneous rapid-sequence cinefluorography is offered with direct or remote viewing.

FLUORICON gives you all of this and more, as you will discover in the following pages. For more detailed information, contact your General Electric representative. He can make arrangements for you to see and try a unit in your area.

GENERAL ELECTRIC



HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA
. . . where a G-E FLUORICON image intensifier provides convenience and flexibility for cinefluorography and daylight (TV) fluoroscopy. While the radiologist observes a monitor in the examining room, others can observe by closed-circuit television elsewhere in the hospital.



AUTOMATIC BRIGHTNESS CONTROL

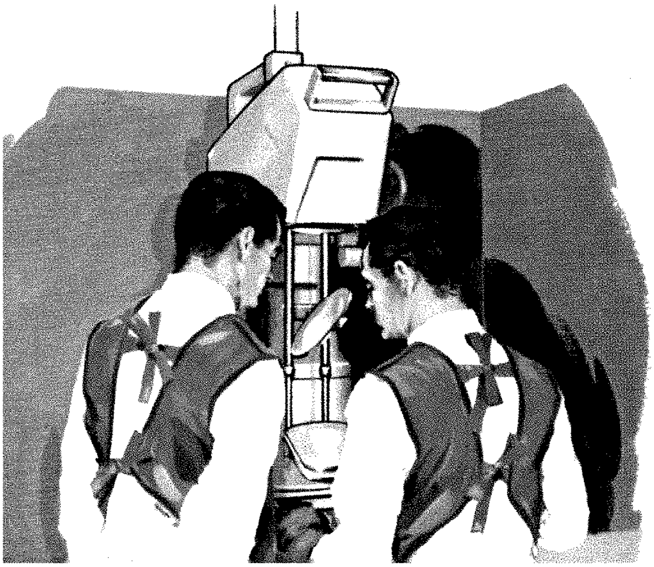
. . . stabilizes the performance of FLUORICON during cinefluorography, TV and direct viewing. In film use you maintain a preselected density through an entire camera run despite variations in patient thickness or opacity. Automatic brightness control functions like a built-in exposure meter that goes to work the instant you start to film.

INSTANTANEOUS CHOICE OF DIRECT VIEWING AND CINE OR TV VIEWING AND CINE

. . . an exclusive FLUORICON feature. No manual manipulating. Just flip one lever to switch from direct viewing to television. During either setting, step down firmly on a footswitch and technic factors automatically shift to preselected values for simultaneous filming.

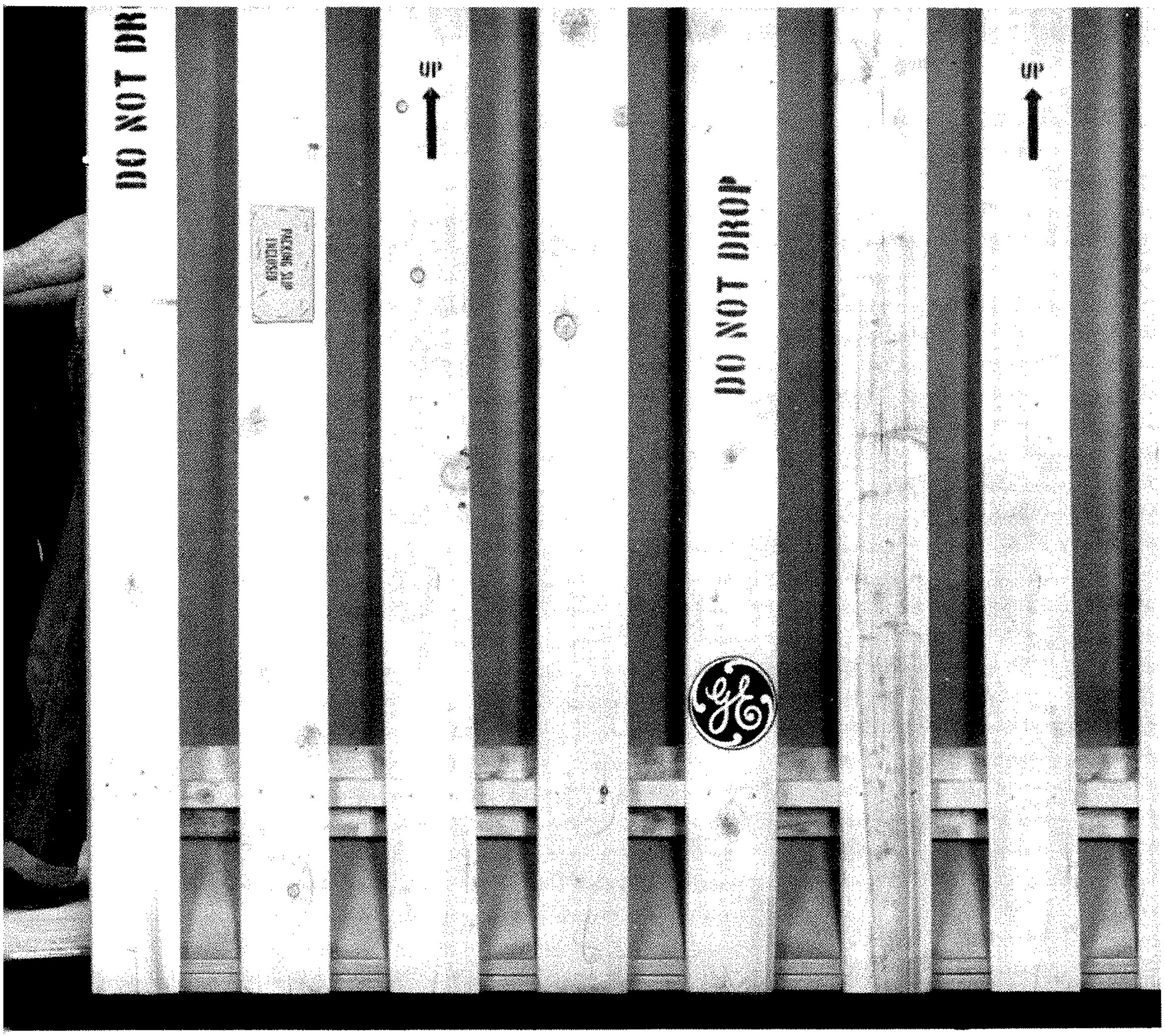
fluoricon

gives you extra facilities..



DISTORTION-FREE OPTICAL SYSTEM

. . . produces a life-size image that you view comfortably, with both eyes, thanks to a generous four-inch exit pupil which allows a latitude for the eye-image relationship without compromising image quality. System provides full viewer brightness even during cine exposure. Enough brightness so two can view simultaneously simply by attaching a beam-splitting consultation mirror.



valuable extra!

services, from pre-installation planning to post-installation technical service. *All are extras you come to count on.*

General Electric representatives know your needs, down to everyday details — how to draw up a technic chart for you; or how to hold technic classes for x-ray personnel when the occasion arises. They supply an impressive array of information on request; basic literature . . . radiological reprints . . . charts, and graphs. And they are always "on call" to help you solve your day to day x-ray problems.

Look beyond the price tag

The services and guidance of qualified representatives should be considered as a part of any x-ray purchase. "After sale" interest from General Electric sees you through the life of your equipment — helps you protect your investment and realize the utmost security of purchase. *Just as with any sound investment, time repays foresight with dividends!*

"compare total cost"

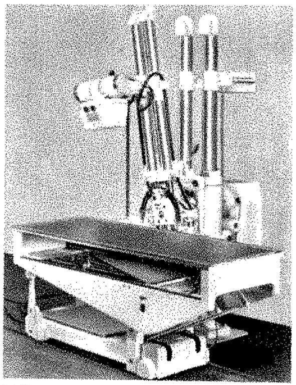
TIME IS THE TRUE TEST OF G-E VALUE

Progress Is Our Most Important Product

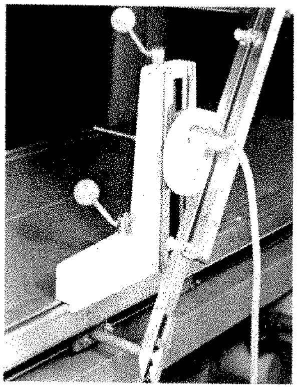
GENERAL ELECTRIC

THE **widest** RANGE EVER IN TOMOGRAPHIC EQUIPMENT!

ALL OF IT **PHILIPS**



MT 2 – Top class, top notch universal motordriven tomograph. Recommended for all high standard routine tomography.



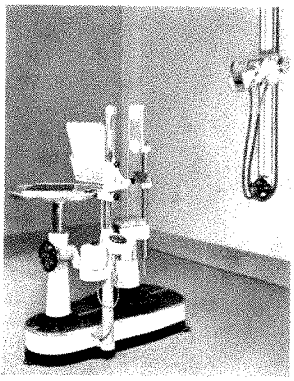
PLANIGRAPHIC ATTACHMENTS are available for adding to bucky tables or other diagnostic units.

ALSO AVAILABLE:

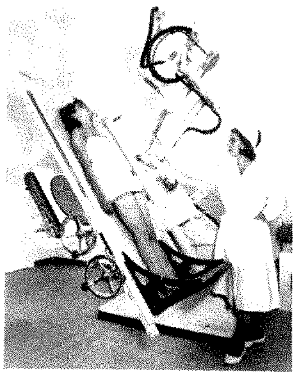
PNEUMOTOME – Tomograph and a vertical stand for chest work, in one unit.
Recommended for chest sanatoria and specialized clinics.

DANATOME – Universal tomograph in a strictly utilitarian price class.
Recommended for heavy work loads where budgets are tight.

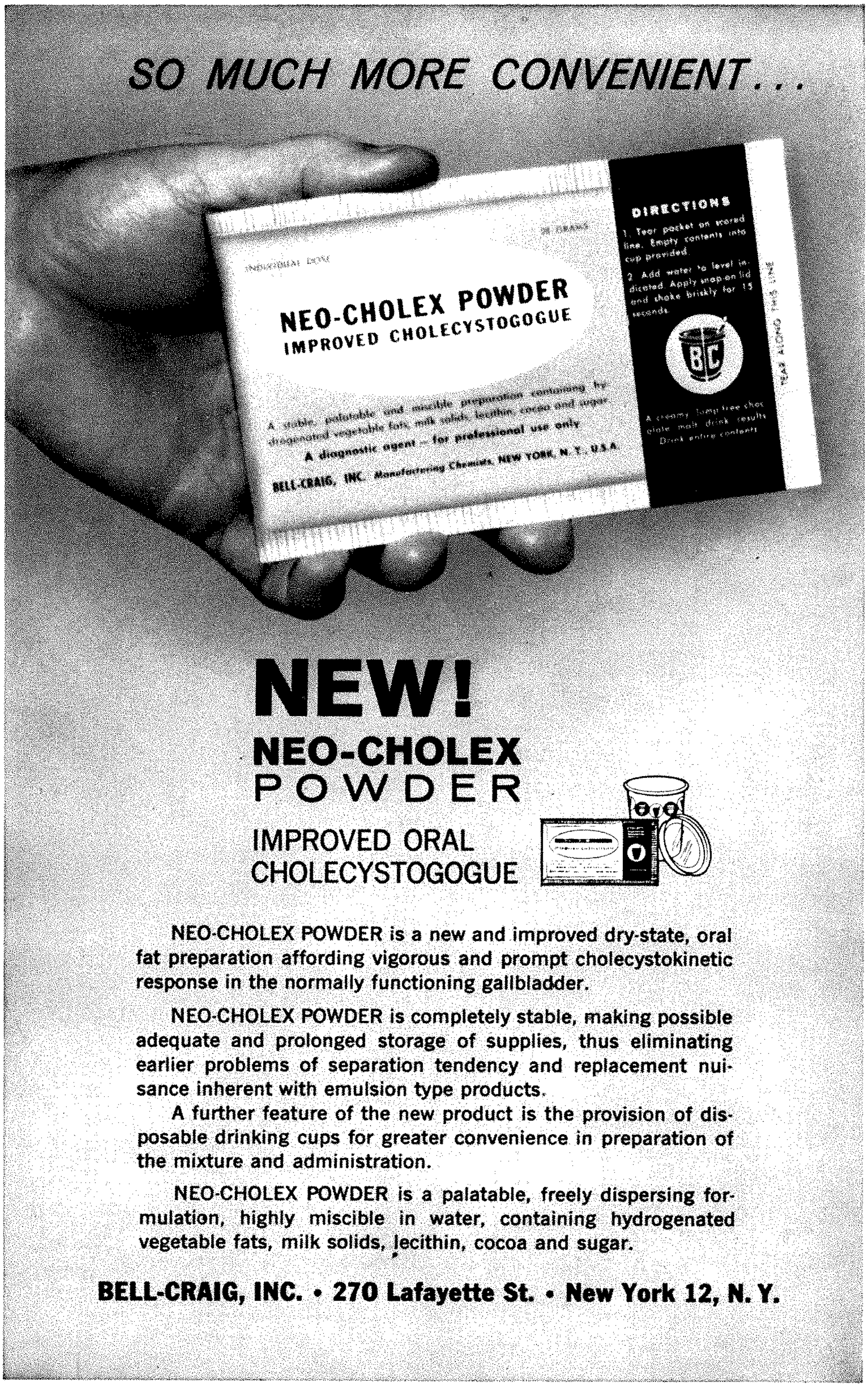
RADIOTOME – Tomograph for visualizing transversal layers. Recommended for therapy departments and for chest tomography of children.



POLYTOME – Precision tomograph that has yet to meet its peer. Recommended for connoisseurs: most definitely when the accent is on bone tomography.



For further information please apply to the Philips organisation in your Country. Sold in the U.S.A. by: North American Philips Company, Inc., Medical & Dental Division, 100 East 42nd Street, New York 17, N.Y.



SO MUCH MORE CONVENIENT...
NEO-CHOLEX POWDER
IMPROVED CHOLECYSTOGOGUE
A diagnostic agent — for professional use only
BELL-CRAIG, INC. Manufacturing Chemists, NEW YORK, N. Y., U.S.A.
DIRECTIONS
1. Tear pocket on scored line. Empty contents into cup provided.
2. Add water to level indicated. Apply snap-on lid and shake briskly for 15 seconds.
BC
A creamy lump-free chocolate malt drink results. Drink entire contents
TEAR ALONG THIS LINE

NEW!

NEO-CHOLEX
POWDER

IMPROVED ORAL
CHOLECYSTOGOGUE

NEO-CHOLEX POWDER is a new and improved dry-state, oral fat preparation affording vigorous and prompt cholecystokinetic response in the normally functioning gallbladder.

NEO-CHOLEX POWDER is completely stable, making possible adequate and prolonged storage of supplies, thus eliminating earlier problems of separation tendency and replacement nuisance inherent with emulsion type products.

A further feature of the new product is the provision of disposable drinking cups for greater convenience in preparation of the mixture and administration.

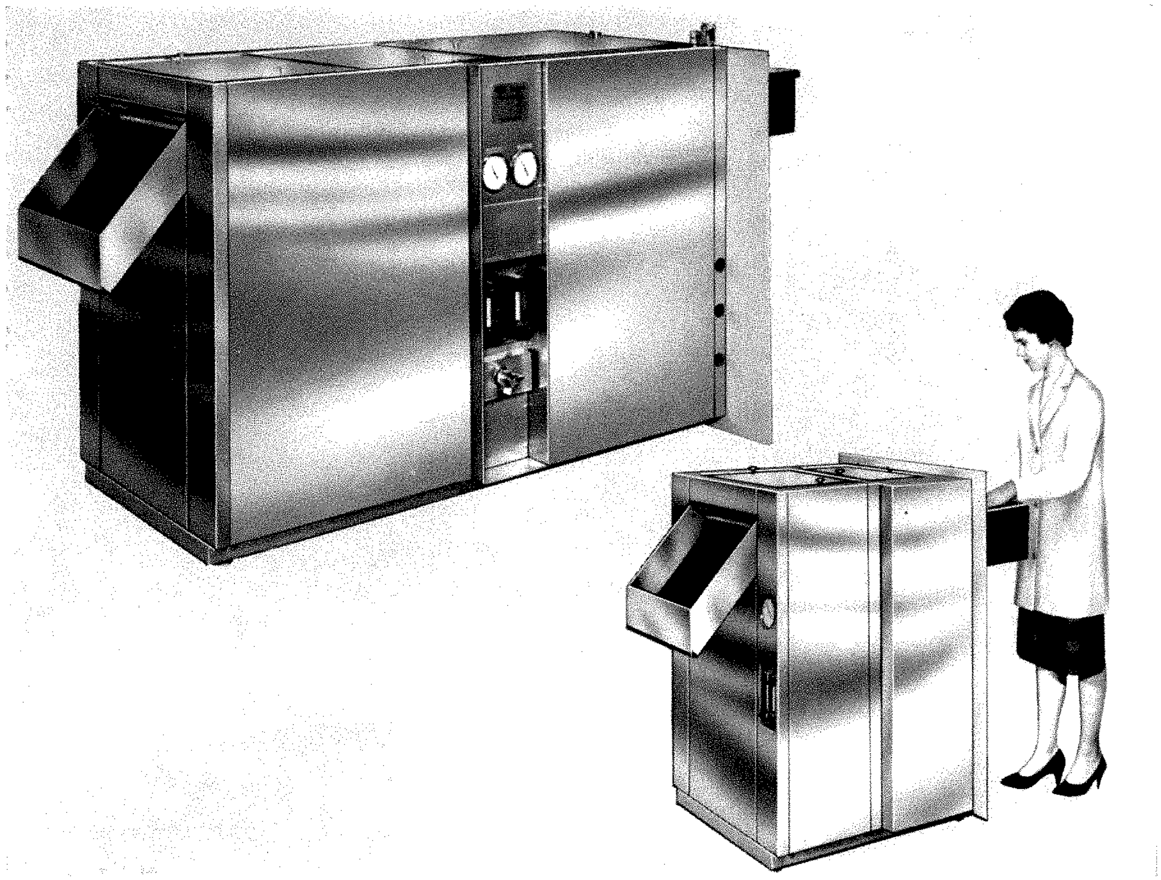
NEO-CHOLEX POWDER is a palatable, freely dispersing formulation, highly miscible in water, containing hydrogenated vegetable fats, milk solids, lecithin, cocoa and sugar.

BELL-CRAIG, INC. • 270 Lafayette St. • New York 12, N. Y.

Hunt know-how gets to the heart of processing problems

Demands of modern x-ray and cine roentgenographic processing require dependable and knowledgeable specialists. Rely on Hunt for a technically oriented sales force, backed up by the Hunt Technical Services Laboratory and roller process service engineers. This depth of service plus the inherent quality of Graph-O-Mat® Developer-Replenisher and Graph-O-Mat® Fixer are the reasons why more and more x-ray departments are switching to Hunt.

PHILIP A. HUNT COMPANY



There's A Size Pakorol to Fit Your Needs, Space and Budget

Automatically processes and drys X-Ray film

Pakorol—Answer to Quality Results, Fast

Minneapolis, Minn.—Hospitals, clinics and even the smallest X-ray offices can now enjoy the benefits of automatic X-ray film processing. The larger Pakorol-X and the small Pakorol-XM each offer a fast, complete, automatic roller-type processing system at a low cost.

Fast, high quality processing and drying

The PAKOROL-X will process 120, 14" x 17" radiographs per hour—the PAKOROL-XM processes 65 14" x 17" radiographs per hour—all with uniform quality.

Space Limitations No Problem

The Pakorol-XM (miniature) is so small, neat and economical, multiple installations have often proven to be the answer to efficiency, speed and cost cutting.

Ultimate in Functional Construction

Some of the many reasons the Pakorol-X and XM drew crowds at recent conventions are: Full worm and gear driven racks, no chains; quiet roller type operation; 6½ minutes processing time (Pakorol-X) 7 minutes (Pakorol-XM) Right and Left hand models; large capacity; processes all brands of medical screen film in sizes 4" x 4" through 17" x 36" and roll film in widths of 17" or less; No. 4 satin stainless steel finish.

Parts, Service, Training

PAKOROL EQUIPMENT is backed by established Pako Parts and Service programs. User training courses are offered regularly at the Pako factory. Let the Pako Planning Service show how the Pakorol-X and the Pakorol-XM will fit your X-ray Department. A suggested layout, tailored to your requirements and space will be prepared upon request, at no obligation.

Clip and Mail Today
Please send complete data on—

☐ PAKOROL-X ☐ PAKOROL-XM

NAME ____________________

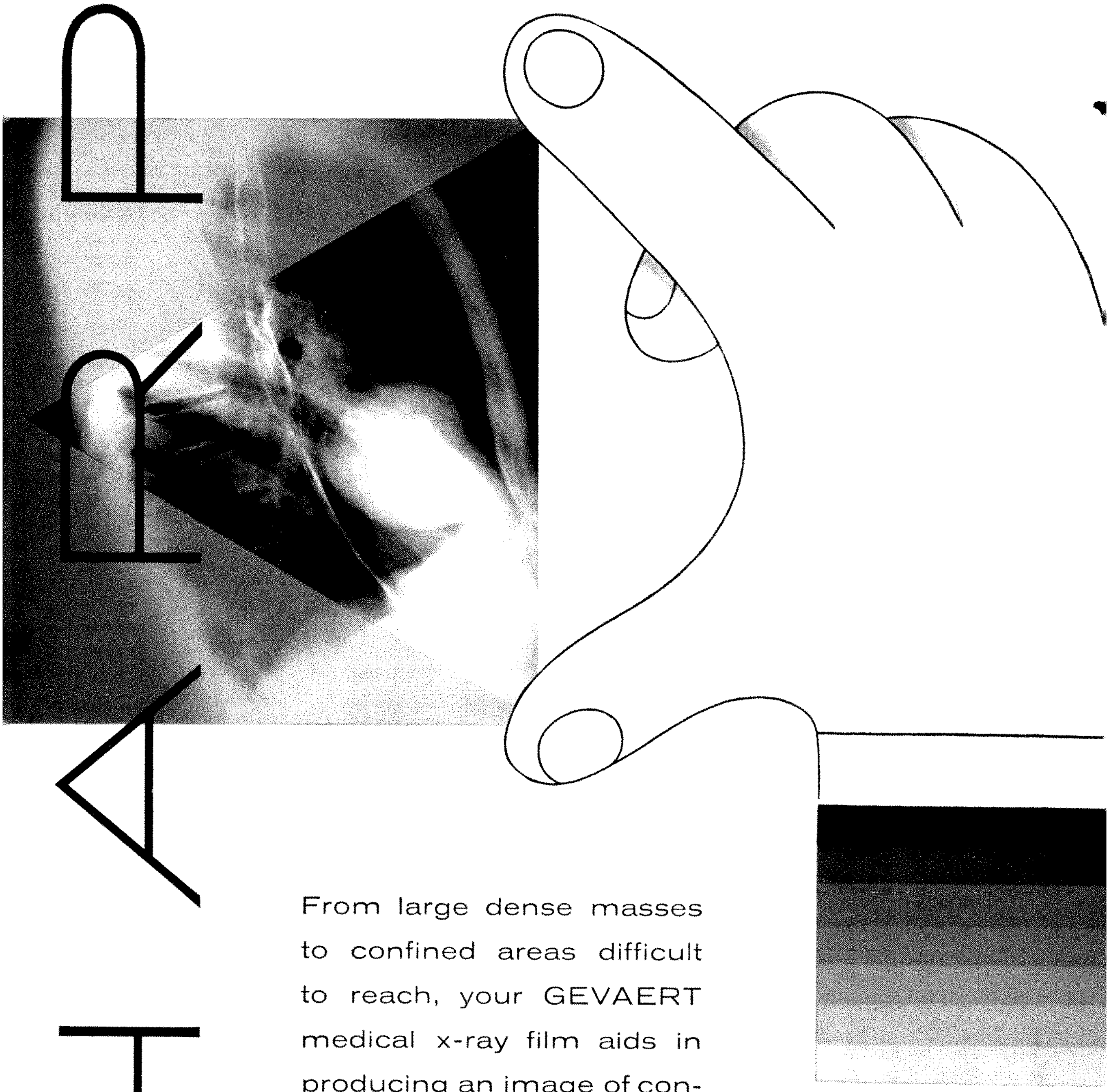
HOSPITAL OR CLINIC ____________________

ADDRESS ____________________

CITY ____________ STATE ____________

PAKO

PAKO CORPORATION
6300 Olson Memorial Highway
Minneapolis 40, Minnesota, U.S.A.
PAKO FOR PROGRESS



From large dense masses to confined areas difficult to reach, your GEVAERT medical x-ray film aids in producing an image of concise clarity and definition. And you achieve this maximum performance with a minimum of exposure.

Exclusive Distributors:
LOW X-RAY CORPORATION
161 Sixth Avenue, New York 13, N.Y.

Other Offices:
2304 Sawtelle Blvd., Los Angeles 64, Calif.
501 Armour Circle N.E., Atlanta 9, Georgia
7307 Ardmore Street, Houston 21, Texas
6611 No. Lincoln Ave., Chicago 45, Illinois

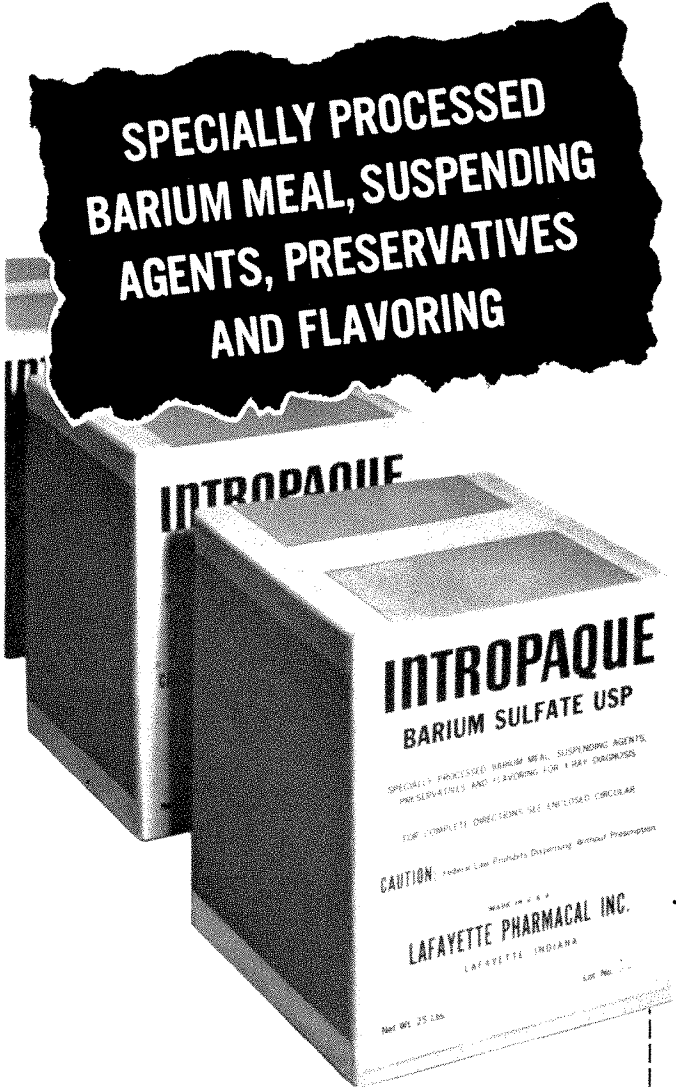
Nationwide Warehousing

GEVAERT
X-RAY FILM

FOR X-RAY DIAGNOSIS...

INTROPAQUE

BARIUM SULFATE, U.S.P. 91%



SPECIALLY PROCESSED BARIUM MEAL, SUSPENDING AGENTS, PRESERVATIVES AND FLAVORING

This highly-processed formula was developed to satisfy multiple criteria for an ideal suspension, and has optimum particle size.

- ▶ Gives a smooth, even coating to the stomach, small bowel, and colon.
- ▶ Will not dry or "flake" in the colon for an hour or more allowing re-examination on same visit.
- ▶ Non-foaming, stable formula allows excess suspension to be saved and used another day.
- ▶ Will not precipitate or agglutinate in the stomach to cause factitious lesions.
- ▶ Remarkable ability to overcome pylorospasm.

Mail Coupon Today for FREE Sample ▶

Lafayette Pharmacal, Inc.
Lafayette, Ind.
Please send me a free sample of Intropaque.
Name____________________
Hospital____________________
Address____________________
City__________Zone___ St.______

LAFAYETTE PHARMACAL INC. LAFAYETTE, INDIANA

Put these New Books in Roentgenolog
to work for you

A STUDY GUIDE FOR STUDENT X-RAY TECHNICIANS

by **Joyce Oliphant,** *Macon Hospital, Macon, Ga.* Based on many years of successful teaching experience, this guide consists of self-testing questions on every phase of x-ray technology . . . *ethics, nursing procedures, contrast medias, terminology, prefixes and suffixes, anatomy and physiology, darkroom, radiographic quality, physics, radioactive substances, radiation protection, routine radiography, special procedures, and positioning.* For answers the student may refer to his classroom lectures and to an excellent list of textbooks and handbooks contained in the study guide. The student who has completed this course of study will be well prepared for his Registry examination. The book will be equally useful to instructors who wish to check their students' progress. *Oct. '63, 168 pp., $5.50*

AN ATLAS OF VASCULA
RINGS AND RELATE
MALFORMATIONS O
THE AORTIC ARC
SYSTE

by **James R. Stewart, Owings W. Kincaid,** *a*
Jesse E. Edwards, *all of the Mayo Clinic, Roch*
ter, Minn. The developmental, anatomic, and dia
nostic aspects of vascular rings and all relat
malformations of the aortic arch system are co
ered in this one comprehensive text and atl
It is the first book devoted entirely to this gro
of malformations—a book of special interest
the radiologist. Following a discussion of develo
ment of the normal aortic arch system, the autho
cover embryologic aspects of congenital malform
tions of the aortic arch system, classification
anomalies, pathologic anatomy, radiologic dia
nosis, and clinical and surgical aspects of vario
lesions. Over 200 drawings, photographs of path
logic specimens, roentgenograms, and angiogra
are included. *Oct. '63, 184 (8½ x 11) pp., 261 i*
$10.

CALCIFICATIONS OF THE HEART

by **Jerome H. Shapiro, Harold G. Jacobson,** *and* **Berta M. Rubinstein,** *all of Montefiore Hospital, New York City;* **Maxwell H. Poppel,** *New York Univ., New York City; and* **John B. Schwedel,** *Montefiore Hospital. With a Contribution on* **Cineradiography** *by* **Joseph Jorgens,** *Univ. of Minnesota, Minneapolis, Minn.* Designed primarily for radiologists . . . to make them aware of the importance of accurately localizing and diagnosing calcifications in and about the heart. *From the uncommon to the common—a variety of calcifications are considered.* Pathology and clinical findings are presented. Roentgen findings are carefully described and profusely illustrated with especially prepared LogEtronic reproductions. Roentgen technique considered extends from simple roentgenography to cineradiography of the heart. *Sept. '63, 208 pp. (7 × 10), 133 il., $12.50*

THE CHEST FILM I
MASSIVE PULMONAR
EMBOLIS

by **Daniel J. Torrance, Jr.,** *The Johns Hopki*
Univ., Baltimore, Md. Covers the x-ray diagno
of massive pulmonary artery occlusion bas
heavily on findings in the plain chest film. T
book consists of twenty-three case presentations
which chief emphasis is on abnormality of ves
shadows in the lung and as exact as possible
correlation between shadows of the vessels on t
x-ray film and actual pathological processes und
lying. Cases are grouped according to morpholo
changes in the vascular shadows—**a groupi**
which has resulted in the emergence of well-defin
patterns sufficiently characteristic to warrant dia
nosis with great assurance. *Oct. '63, 88 pp. (8*
× 11), 76 il. (Amer. Lec. Roentgen Diagno.
edited by Lewis E. Etter, Univ. of Pittsburg
$6.75

CHARLES C THOMAS • PUBLISHER 301-327 East Lawrence Avenue **SPRINGFIELD • ILLINO**

RALPH M. CAULK, M.D.

THE AMERICAN JOURNAL
OF ROENTGENOLOGY
RADIUM THERAPY AND
NUCLEAR MEDICINE

VOL. 90 DECEMBER, 1963 No. 6

ON THE PRESERVATION OF AN IMAGE*

THE PRESIDENT'S ADDRESS

By RALPH M. CAULK, M.D.
WASHINGTON, D. C.

THE investiture which you have just witnessed represents the conference of an honor of which a recipient can be justifiably proud and humbly grateful. In this respect, your President is as much a conformist as is humanly possible. It is hoped that the affairs of this office will be authoritatively conducted and that the faith of the Society has not been entirely misplaced. This opportunity is also taken to thank those who have worked hard in making the preparations for the Sixty-fourth Annual Meeting of the American Roentgen Ray Society, and thereby assuring its success.

In most of the areas where one works as President-Elect of this Society, help is available and is, in fact, mandatory. I, therefore, reviewed the remarks of the more recent presidents, in order to find the motivating factors behind their illustrious presentations. References to motivation were made in two instances: Dr. Reineke stated, "Traditionally an inaugural address should point with pride or view with alarm the accomplishments or shortcomings of the organization or the profession involved." He went on to state that he preferred to do neither and proceeded with a most astute, timely and well conceived presentation. Dr. Dabney Kerr noted as follows: "It is the custom for the incoming president of the Society to discourse on a subject in which he is particularly interested."

The subject which I have chosen recognizes great accomplishments as well as certain areas which might be considered alarming, and is one in which I am indeed most interested. It is titled, "Preservation of an Image." The term "image" may have scientific connotations for radiologists in connection with their day by day association with fluoroscopy, image intensification, roentgenography and more recently television radiology. The "image" to which I refer is also a constant day by day affair, and to me a very important one to perpetuate. It is the "image" which we, as radiologists, present to those people with whom we become associated in our daily work.

Doctor image to patients. In previous addresses much emphasis has been placed by the various speakers on asserting the doctor aspect of radiology and the need for recognition of the radiologist as a clinician. Actually, so much time has been devoted to this subject, not only before this Society but elsewhere, that one may wonder at times as to whether or not we are inadvertently assuming a defensive attitude.

---

* Presented at the Sixty-fourth Annual Meeting of the American Roentgen Ray Society, Montreal, Quebec, Canada, October 8–11, 1963.

It is extremely important that the radiologist's "image" to the patient as a physician and clinician be promoted and maintained. In case one feels secure in this matter, one needs only to ask patients where their previous radiologic work was carried out and by whom. In all too many instances, one finds that the patient does not know who conducted this valuable clinical study and/or treatment. We, as radiologists, have throughout the working day the opportunity to impress upon patients the clinical aspect of our specialty and thus augment and perpetuate this very significant doctor "image."

Doctor image in third party insurance plans. This is an economic field with which we are all familiar and in which we are constantly involved. It is concerned with an erroneous philosophic concept prevalent in many areas, not necessarily physical, which briefly stated is as follows: (a) Radiology, as practiced in hospitals, is a hospital rather than a medical service; and (b) hospital radiology is a symbol of quality control in direct contrast to office radiology in which this quality may be open to question.

These concepts have been brought about by a lack of vigilance on the part of many of us and our predecessors in the initial acceptance and promotion of radiologic benefits underwritten by Blue Cross rather than by Blue Shield plans. The failure to preserve our identity as physicians entrusted with the medical care of patients has aided in the audacious propagation of this concept. Often by sheer neglect we have missed opportunities to introduce ourselves into areas where our influence can be strong in giving aid, advice and management to various third party plans.

The radiologist's image as a scientist. One need go no further than to attend this annual meeting of our Society and to read our Journal to realize that radiology, as a specialty in medicine, has an enormous scientific component. *This* concept must be maintained. Interest in the scientific aspect of medicine must be evinced at propitious moments whenever possible, whether it be a presentation before a specialty group, County Medical Society, Hospital Staff Meeting or in the course of ordinary daily consultative procedures.

The radiologist's image in organized medicine. It is always refreshing to note the appointment to committees or the election to office of radiologists in local, county, state and national medical organizations. This applies also to committee and organizational work on the staff of hospitals. One of the virtues of the many professional contacts which are inherent in the practice of radiology is that it qualifies the radiologist well for these duties and radiologists should endeavor to contribute their share of work in these areas.

The radiologist's image in hospital radiology relationships. The professional and ethical stature of the radiologist in hospital relationships should be such that he should not have to seek shelter under the manifestoes issued by organized medical bodies which reiterate the fact that radiology is the practice of medicine and *ipso facto* we are made doctors by *fiat.*

In concluding this address, I wish to state that the foregoing is not the complete picture of the "image" concept, but the examples cited serve to show us the importance of being eternally vigilant, impeccably honest and professionally competent if we are to enhance and perpetuate the ideals and good works of the American Roentgen Ray Society and other scientific radiologic societies, the American College of Radiology and the American Board of Radiology. A vast amount of time and energy has been spent by the leadership in the above areas in an endeavor to create a good image for us. To say it idiomatically, "We have a lot of good things going for us. Let us keep it that way."

Washington Hospital Center
110 Irving Street N.W.
Washington 10, D. C.

Vol. 90, No. 6

SOME NEW PORTABLE RADIOACTIVE SOURCES FOR DIAGNOSTIC RADIOGRAPHY

By KENNETH L. KRABBENHOFT, M.D.,* *and* FARNO L. GREEN, M.S.†
DETROIT, MICHIGAN

RADIOGRAPHY with portable radioactive isotope sources producing acceptable diagnostic quality is reported in this paper. Of particular importance is the experience gained in chest radiography since this represents the first such study in which successful diagnostic examination of the chest has been accomplished. The importance of chest radiography is underscored by the extent of survey programs conducted for the purpose of detecting pulmonary disease. Pulmonary tuberculosis has been a scourge of mankind since time immemorial and there is a high incidence of this disease in remote areas of the world. The development, therefore, of a portable source of energy, independent of an electrical power supply and permitting large scale surveys, may prove to be of substantial value.

Herein, the first acceptable chest radiograph exposed for diagnostic purposes with a radioactive source, ytterbium 169 (Yb^{169}) which has a half life long enough to fulfill the above requirements for use in remote areas, is described.

The advantages of portable sources of radiation for obtaining diagnostic radiographs are many. Portable roentgen ray units have been devised to be operated with small generators or batteries, but they are still dependent upon a primary source of electrical energy. They also have a limited useful tube life and other technical disadvantages due to electrical maintenance requirements which would be especially troublesome in remote areas. Consequently, sources independent of electrical energy for field use in remote areas, or in time of disaster, would be most desirable. A radioactive isotope source would provide such freedom since constant photon energy and freedom from source failure are inherent in isotope sources. A small, light-weight portable source, housed in a suitable exposure and storage device, has flexibility and mobility and its storage problems are minimal.

Another advantage is the ability to place a small portable source within a body cavity and thus expose a film external to the body. Theoretically, this would obviate the overlapping of confusing structures and permit the examination of some structures which are now relatively inaccessible.

Basic requirements for radioactive isotopes to be suitable for radiography are the emission of photons with energies predominantly of 30–150 kev., high specific activity and relatively long half life or useful life. The relationship of the important factors of energy, source output and half life, is the subject of a recent report by Green.[5]

In the past, studies of the feasibility of applying radioactive sources to diagnostic radiography have centered primarily around thulium 170 (Tm^{170}) because of the low energy components of its radiation spectrum and its reasonable half life. The major disadvantages of Tm^{170} and other previous sources were, in most cases: (1) large geometric source size which compromised definition, (2) low radiation intensity which necessitated short source film distances and long exposure times, and (3) in the case of Tm^{170}, undesirable high energy Bremsstrahlung resulting from energetic beta particles. Until newer radioactive sources became available, however, none appeared to be suitable for chest radiography.

---

* Department of Radiology, Harper Hospital, Detroit, Michigan.

† Formerly with Research Laboratories, General Motors Corporation, Warren, Michigan; Present address: Viso Corporation, Detroit, Michigan.

Presented at the Sixty-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 2–5, 1962.

The present study, using 5 different radioisotopes, is the first extensive clinical evaluation of isotope radiography to be reported. Numerous anatomic parts in addition to the chest were examined. In order to judge the diagnostic accuracy of isotope radiography, comparisons were made with conventional roentgenographic studies.

HISTORY

Spangenberg[22] made one of the earliest uses of isotope radiography by placing a small radioactive cesium* source within the oral cavity (Table I). Subsequent applications of this technique were made by Mayneord[13] using Tm^{170} and, more recently, by Beronius, Forberg, Henrikson and Söremark,[1] who employed I^{125}. However, the exposures have been lengthy and clinically impractical or impossible.

Thulium 170 has been the most extensively investigated isotope source to date with most studies directed to thin body sections such as the hand, foot, and ankle, due to relatively small source strengths. The exposures with this isotope have also been rather long in most instances, the shortest being reported by Ireland[10] and Burke[2] (Table I). Ireland achieved short exposure times using xenon 133 (Xe^{133}) which has a half life of 5.3 days. Furthermore, a short source film distance of 30 cm. (about 12 in.) was used.

The attempts to employ other isotopes, such as americium 241 (Am^{241}) by West,[26] Xe^{133} by Mayneord and Ireland,[15] beta-excitation radiography with strontium 90 (Sr^{90}) by Krebs and Kereiakes,[11] cerium 144 (Ce^{144}) by Dennis and DeLuca[4] and Spangenberg and Pool,[24] as well as numerous other works based on the use of Tm^{170}, are documented in Table I. This is a compilation of studies published on isotope medical radiography known to the authors and includes some unpublished studies by Nurnberger[17,18] using samarium 153 (Sm^{153}) and Yb^{169}. Representative exposures from the present study made with Yb^{169} radiography of various anatomic parts are listed for comparative purposes. The use of a very low intensity iodine 125 (I^{125}) source in solution was reported by Myers.[16] Beronius, Forberg, Henrikson and Söremark[1] employed a 12 mc I^{125} source for dental and extremity radiography.†

MATERIAL AND METHODS

In the present study Tm^{170} and 4 isotopes heretofore not utilized for clinical radiographic application were evaluated. They are Sm^{153}, gadolinium 153 (Gd^{153}), Yb^{169} and lutetium 177 (Lu^{177}). Table II shows the total number of exposures made with various sources to indicate the quantity of accumulated data. A concentrated clinical study of extremities with Yb^{169} sources was made for comparison with numerous cadaver studies made previously but not included in this table. The large number of exposures made with Yb^{169} indicates the emphasis placed on chest radiography.

A radiographic exposure device was constructed using tungsten alloy for shielding. With this unit exposures as short as 0.1 second can be accurately timed. Its weight of 26 pounds renders it easily portable.

Furthermore, numerous experimental data from many exposures have been accumulated and the influence of technical factors, such as grid, variability of exposure time and short source film distance was investigated.

In our present experience the reduction of exposure times to fractions of seconds has been possible with ytterbium 169, employing an 18 inch source film distance for thin body sections (Fig. 2 *A*).

COMPARISONS OF VARIOUS ISOTOPES

The source characteristics of the 5 isotopes evaluated are listed in Table III.

---

* Designated in the reference as "radioactive cesium," but symbol given for the element was "Ce^{139}" (cerium 139). Therefore it is unclear whether an isotope of cerium or cesium was used.

† In January, 1963 we achieved I^{125} radiography of the hand with an exposure time of approximately 2 minutes using a solid source and a source film distance of 18 inches.

TABLE I

RADIOGRAPHY WITH RADIOACTIVE SOURCES—1948 TO 1963

Reference	Year	Source					Object (thickness)	Technique				Exposure Time	Air-Skin Dose (calculated)	Comments
		Isotope	Size	Age	Activity	Output		Source Film Distance	Film	Screen	Grid			
Spangenberg, H. D., Jr.[22]	1948	Ce^{139}(?)	x (not stated)	x	x	x	Teeth	x	Dental	x	x	x	x	Dried maxilla, no exposure data given (See footnote, p. 1124)
Mayneord, W. V.[13]	1952	Tm^{170}	3 mm. dia.	x	x	0.08 mrhm (calc.)	Mandible (Lat.)	12 cm.?	x	No	x	10–11 hr.	x	Dried specimen
							Skull	12 cm.?	x	Yes	x	1 hr.	x	Fig. 1, p. 277, source center of buccal cavity—dried specimen
							Maxilla, mandible	x	x	x	x	x	x	Fig. 2, p. 277, source center of buccal cavity—dried specimen
							Hand (PA)	6 cm.	x	x	x	5 min.	x	Fig. 3, p. 278
Spangenberg, H. D., Jr., and Pool, M. L.[22]	1953	Cs^{131}	0.7 mm. dia.	< 9.6 da.	x	x	Teeth	4 cm.	Dental	x	x	11 hr.	x	Fig. 3, p. 628, dried skull
				> 9.6 da.	x	x	Maxilla, mandible, facial bones	4 cm.	x	x	x	1 wk.	x	Fig. 4, p. 629, dried skull
West, R.[25]	1953	Am^{241}	3.2 c/gm.	x	6 mc	x	Femur (AP)	6 in.	Ilford Industrial Type C	x	x	60 hr.	x	Dried specimen
Untermyer, S.[26]	1954	Tm^{170}	200 mg.	x	x	2,000 mr/hr. @ 1 ft.	Hand (PA) Ankle (Lat.)	30 in.	Kodak Blue Brand	Par Speed	Yes	x	x	Without lead cassette backing
Hasterlik, R. J.[9]	1954	Tm^{170}	200 mg.	x	x	75,000 mr/hr. @ 1 in.	Hand (PA) Ankle (Lat.)	15 in.	Kodak Blue Brand	Par Speed	No	30 sec.	x	With lead cassette backing (best result)
Dennis, G. E., and DeLuca, H. A.[4]	1954	Tm^{170}	0.375 in. (170 mg. with 48% Tm_2O_3)	x	5 c	15 mrhm	Hand (PA)	11 in.	x	Hi-Speed	x	2 min.	8 mr	Fig. 1, p. 662—patient
					5 c	15 mrhm	Hand (PA)	22 in.	Non-screen	No	x	60 min.	60 mr	Fig. 2, p. 662—cadaver
					5 c	15 mrhm	Elbow (AP)	22 in.	Non-screen	No	x	60 min.	60 mr	Fig. 3, p. 663—cadaver
					x	x	Shoulder (AP)	x	x	x	Yes	x	x	Lacking definition and contrast
		Ce^{144}	0.5 in. walls	x	150 mc	x	Hand (PA)	24 in.	x	No	x	17 hr.	x	Fig. 4, p. 663—cadaver
					150 mc	x	Skull—molars	12 in.	x	No	x	1 hr.	x	Dried skull with wax to simulate soft tissue
		Ce^{144}	0.375 in. dia.	x	15 c	x	Hand (PA)	21 in.	x	No	x	30 min.	x	Fig. 5, p. 664—cadaver
							Hand (PA)	21 in.	x	No	x	30 min.	x	Fig. 6, p. 664—cadaver
Shemesh, A., and Rice, W. E.[20]	1956	Tm^{170}	x	x	70 c	6,800 mr/hr. @ 1 ft. (see comment*)	Hand (PA)	19 in.	Du Pont Extra fast	Medium Speed	No	30 sec.	x	Fig. 4, p. 10 (possible error in exposure time noted on film compared to legend)
							Ankle (Lat.)	19 in.	Du Pont Extra fast	Medium Speed	No	30 sec.	x	Fig. 6, p. 12 * Apparent discrepancy in curie value or output based on commonly accepted values
Coleman, E. W.[3]	1956	Tm^{170}	4.3 mm. dia. × 3 mm. ht. (399 mg.)	x	120 c ± 20	700 mrhm (see comment*)	Extremities—8 in.	19 in.	x	x	x	10–30 sec.	26–78 mr	No radiographs—thought to be inferior to electronic machine but acceptable for foreign body localization * Calculated from value of 3.12 r/hr. @ 19 in. given. However, accepted values for Tm^{170} of 2.5–3.5 mrhm/c would give 300 mrhm

TABLE I—(*Continued*)

Reference	Year	Source					Object (thickness)	Technique				Exposure Time	Air-Skin Dose (calculated)	Comments
		Isotope	Size	Age	Activity	Output		Source Film Distance	Film	Screen	Grid			
Burke, D. E.[2]	1956	Tm^{170}	x	New	x	x	Kidney	7 in.	x	Super Speed	x	1 to 5 sec.	x	Fig. 7 and 8, p. 514. Source of information not stated
							Wrist (AP) Wrist (Lat.)	7 in. 7 in.	x x	Super Speed	x x	13 sec. 15 sec.	x x	Fig. 9, p. 515. Colles' fracture, plaster cast, 1 cm. thick
Mayneord, W. V., and Ireland, H. J. D.[15]	1956	Tm^{170}	2 mm. dia. ×2 mm. long (35 mg. Tm_2O_3 sintered oxide)	x	2 c (est.)	450 mr/hr. @ 10 cm.	Mandible (AP)	10 cm.	Ilford Red Seal	Ilford H.V.	No	20 sec.	x	Fig. 4, p. 279, dried specimen
							Mandible (AP)	10 cm.	Ilford Red Seal	Ilford tungstate	No	34 sec.	x	No difference in radiographic quality, compared with H.V. screens—dried specimen
							Mandible (AP)	10 cm.	Ilford Red Seal	No	No	800 sec.	x	Improvement in definition but prohibitively long exposure—dried specimen
							Various objects	25 cm.	Ilford Red Seal	x	Lysholm	double over no grid	x	No improvement in definition
							Various objects	x	Ilford Red Seal	x	Potter-Bucky	double over no grid	x	Slight improvement
							Hand (PA)	10 cm.	Ilford Red Seal	Ilford H.V.	No	45 sec.	x	Fig. 6, p. 280
							Mandible (AP)	80 cm.	Ilford Red Seal	Ilford H.V.	No	144 min.	x	Fig. 7*A*, p. 280 (Tm^{170}) compared to Fig. 7*B*, p. 280 (roentgenogram). Contrast much lower with Tm^{170}
		Roentgen ray	(for comparison)	x	x	75 kv.; 10 ma.	Mandible (AP)	80 cm. (TFD)	Ilford Red Seal	Ilford H.V.	No	0.02 sec.	x	
		Xe^{133}	Charcoal grain 1.5×2.0 mm.	x	1.5 c	25 mr/min. @ 30 cm.	Mandible (AP)	5–10 cm.	Ilford Red Seal	Ilford H.V.	No	x	x	Fig. 11, p. 283. Source inside mouth, short exposure time compared to time required for placement of source
						13 mr/min. @ 30 cm.	Ankle (Lat.)	30 cm.	Ilford Red Seal	Ilford H.V.	No	40 sec.	3 mr (on film)	Fig. 12*A*, p. 283
				x	x	x	Ankle (Lat.)	20 cm.	Ilford Red Seal	Ilford H.V.	No	2 min.	x	Fig. 12*B*, p. 283, fractured tibia
			Line source	6 da.	x	68 mr/min. @ 30 cm.	Hand (PA)	22 cm.	Ilford Red Seal	Ilford H.V.	No	3 sec.	x	Fig. 14*A*, p. 284
							Elbow (AP)	22 cm.	Ilford Red Seal	Ilford H.V.	No	8 sec.	x	Fig. 14*B*, p. 284
Krebs, A. T., and Kereiakes, J. G.[11]	1956	Tm^{170}	Pellet 4×4 mm. 400 mg. (citing Carpenter)	x	40 c	x	Hand (PA)	18 in.	Power paper	Yes	No	20 sec.	x	Fig. 5, p. 171
		Sr^{90}	β-excitation	x	x	x	Rat body	12 in.	Kodak Blue Brand	Yes	No	5 min.	x	Fig. 8, p. 172
							Hand (PA)	12 in.	Kodak Blue Brand	Yes	No	5 min.	x	Fig. 9, p. 173
Roberts, J. E.[19]	1956	Tm^{170}	2 mm. tube	x	150 mc	x	Carpal scaphoid (PA)	6 in.	Kodak Blue Brand	Par Speed	No	90 sec.	x	Fig. 1, p. 629
Spangenberg, H. D., Jr., and Pool, M. L.[24]	1957	Ce^{144}	0.094 in. dia. ×0.094 in. length	x	1 c?	1,000 mr/hr. @ 10 in.	Skull (Lat.)	10 in.	x	x	x	6 min.	100 mr	Fig. 1, p. 3, dried specimen
		Sm^{145}	x	x	x	x	Skull (Lat.)	16 cm.	x	x	x	x	62 mr	Fig. 19, p. 25, dried specimen

TABLE I—(*Continued*)

Reference	Year	Source					Object (thickness)	Technique				Exposure Time	Air-Skin Dose (calculated)	Comments
		Isotope	Size	Age	Activity	Output		Source Film Distance	Film	Screen	Grid			
Ireland, H. J. D.[10]	1957	Tm^{170}	Fragment	x	x	x	Skull, mandible	x	Ilford Red Seal	Ilford H.V.	No	10 hr.	x	Fig. 3, p. 264, dried specimen
		Xe^{133}	x	x	x	70 mr/min. @ 30 cm.	Ankle (Lat.)	30 cm.	Ilford Red Seal	Ilford H.V.	No	x	x	Fig. 5, p. 265
							Hand (PA)	30 cm.	Ilford Red Seal	Ilford H.V.	No	3 sec.	x	Fig. 6*A*, p. 265
							Elbow (AP)	30 cm.	Ilford Red Seal	Ilford H.V.	No	8 sec.	x	Fig. 6*B*, p. 265
Green, F. L., Disney, C. T., Cheek, W. D., and Graham, G. P.[8]	1958	Sm^{153}	2 mm. dia. × 2 mm. long	6 da.	1.3 c	100 mrhm	Foot (AP)	18 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	No	20 sec.	2 mr	Cadaver—radiograph of low density
Green, F. L.[6]	1959	Gd^{153}	2 mm. dia. × 2 mm. long	76 da.	x	4 mrhm	Foot (AP)	18 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	No	30 min.	10 mr	Cadaver
				71 da.	x	4 mrhm	Ankle (Lat.)	18 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	No	20 min.	7 mr	Cadaver
		Sm^{153}	2 mm. dia. × 2 mm. long	71 da.	x	3 mrhm	Foot (AP)	18 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	No	3 hr.	36 mr	Cadaver
				281 da.	x	1 mrhm	Ankle (Lat.)	18 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	No	7 hr.	27 mr	Cadaver
		Tm^{170}	2 mm. dia. × 2 mm. long	281 da.	1 c	2.5 mrhm	Ankle (Lat.)	18 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	No	1 hr.	10 mr	Cadaver
Nurnberger C. E.[17]	1960	Sm^{153}	2 mm. dia. × 2 mm. long	6 da.	1 c	70 mrhm	Hand—1.75 in. (PA)	18 in.	Kodak Royal Blue (old)	Hi-Speed	No	30 sec.	1 mr	Fig. 7*A*
				2 da.	6.4 c	450 mrhm	Ankle—2.75 in. (Lat.)	18 in.	Kodak Royal Blue (old)	Par Speed	No	6 sec.	1.5 mr	Fig. 7*B*
							Knee—5 in. (AP)	18 in.	Kodak Royal Blue (old)	Par Speed	No	8 sec.	1.9 mr	Fig. 8*A*
				2 da.	6.3 c	440 mrhm	Skull (Lat.)	30 in.	Kodak Royal Blue (old)	Hi-Speed	No	35 sec.	4.2 mr	Fig. 8*B*
							Shoulder—6 in. (PA)	30 in.	Kodak Royal Blue (old)	Hi-Speed	No	21 sec.	2.5 mr	Fig. 9*A*
				6 da.	1.5 c	105 mrhm	Pelvis—salpingogram	30 in.	Kodak Royal Blue (old)	Hi-Speed	Yes	93 sec.	2.0 mr	Fig. 9*B*
Zodiev, V. V., Dmokhovskii, V. V., and Moslov, L. A.[27]	1960	Tm^{170}	5.5 mm. dia., 1.4 gm./cm.^{2} (2 mm. thick)	x	x	x	Wrist	60 cm.	x	x	x	15 sec.	x	Fig. 3, p. 65, cadaver
							Elbow	60 cm.	x	x	x	20–25 sec.	x	Table 3, p. 64, cadaver
							Knee joint	60 cm.	x	x	x	45–50 sec.	x	Table 3, p. 64, cadaver
Nurnberger, C.E.[18]	1961	Yb^{169}	2 mm. dia. × 2 mm. long	x	8.3 c	295 mrhm	Hand (PA)	18 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	No	3 sec.	1.1 mr (calc. air dose to film)	
							Knee (Lat.)	24 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	Potter-Bucky	60 sec.	10 mr (calc. air dose to film)	

TABLE I—(*Continued*)

Reference	Year	Source					Object (thickness)	Technique				Exposure Time	Air-Skin Dose (calculated)	Comments
		Isotope	Size	Age	Activity	Output		Source Film Distance	Film	Screen	Grid			
							Ankle (Lat.)	24 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	Potter-Bucky	36 sec.	6 mr (calc. air dose to film)	
							Skull (Lat.)	24 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	Potter-Bucky	94 sec.	16 mr (calc. air dose to film)	Poor detail
Beronius, P., Forberg, S., Henrikson, C. O., and Söremark, R.[1]	1962	I^{125}	0.5 mm. dia.	x	12 mc	x	Mandible	6 cm.	Kodak Kodirex	No	No	12 min.	x	Fig. 2, p. 254. Source placed intraorally, dried skull
							Teeth	7 cm.	Kodak Ultra Speed Dental	No	No	60 min.	x	Fig. 3, p. 254, dried mandible
							Hand	20 cm.	Cea Singul-X	No	No	60 min.	x	Fig. 4, p. 254, cadaver
Green, F. L.[5]	1962	Sm^{153}	2 mm. dia. × 2 mm. long	1.5 da.	8.6 c	600 mrhm	Chest—21 cm. (PA)	40 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	No	60 sec.	16 mr	Patient exposure by C. T. Disney, M.D. on 11-24-59. First diagnostically acceptable isotope chest radiograph of living subject
Myers, W. G.[16]	1962	I^{125}	Solution 0.5 mm. dia. × "few" mm. thick	x	4 mc	x	Hand (PA)	50 cm.	Ansco Non-screen	No	No	20 hr. (5 "curie minutes" calc.)	x	Fig. 1, p. 773, cadaver
Lange, W. H., Greene, J. L., Green, F. L., and Graham, G. P.[13]	1963	Sm^{153}	2 mm. dia. × 2 mm. long	x	8 c	540 mrhm	Chest—19 cm. (PA)	48 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	No	20 sec.	3 mr	Fig. 4
		Yb^{169}	2 mm. dia. × 2 mm. long	x	x	x	Hip phantom (Lat.)	20 in.	Kodak Royal Blue (old)	Du Pont Hi-Speed	No	14 hr.	x	Fig. 12
Present study (representative exposures)	1961 and 1962	Yb^{169}	2 mm. dia. × 2 mm. long	2 da.	21 c	740 mrhm	Chest—21 cm. (PA)	48 in.	Kodak Royal Blue (old)	Hi-Speed	No	40 sec.	8.2 mr	First diagnostically acceptable chest radiograph exposed with Yb^{169} source
				12 da.	40 c	1,400 mrhm	Hand—3 cm. (PA)	18 in.	Kodak Royal Blue (new)	Hi-Speed	No	0.75 sec.	1.7 mr	Fig. 2*A*
				6 da.	43 c	1,550 mrhm	Ankle—6 cm. (Lat.)	18 in.	Kodak Royal Blue (new)	Hi-Speed	No	1 sec.	2.5 mr	
				21 da.	31 c	1,080 mrhm	Leg—9 cm. (AP and Lat.)	18 in.	Kodak Royal Blue (new)	Hi-Speed	No	2.5 sec.	7.0 mr	
				36 da.	22 c	780 mrhm	Leg with cast—13 cm. (AP and Lat.)	18 in.	Kodak Royal Blue (new)	Hi-Speed	No	10 sec.	20 mr	Fig. 12, *B* and *D*
				39 da.	20.5 c	720 mrhm	Pelvis—25 cm.	36 in.	Kodak Royal Blue (new)	Hi-Speed	Yes	1 min.	27 mr	Fig. 11
				12 da.	40 c	1,400 mrhm	Skull—16 cm. (Lat.)	36 in.	Kodak Royal Blue (new)	Hi-Speed	Yes	15 sec.	10 mr	Fig. 10
				14 da.	46 c	1,600 mrhm	Chest—21 cm. (PA)	36 in.	Kodak Royal Blue (new)	Hi-Speed	No	1 sec.	1 mr	Fig. 6*B*

Table II

NUMBER OF CLINICAL EXPOSURES WITH VARIOUS SOURCES

(August 23, 1961 to September 20, 1962)

Anatomic Part	Yb^{169}	Sm^{153}	Gd^{153}	Lu^{177}	Tm^{170}
Chest	79	9		10	
Skull	20				
Hand	15		5		4
Leg	12				
Ankle	8	4			
Pelvis	7				
Cervical Spine	2				
Abdomen	2				
Total	145	13	5	10	4

Their half lives, photon energies and source strengths are compared with cobalt 60, a more familiar isotope. Figure 1 *A* shows the continuous spectra of x-ray energies commonly used in roentgenography, 65 kv. and 150 kv., for comparison to the spectra of the isotopes studies. In Figure 1 *B* the spectrum of Sm^{153} is seen to be composed of 42, 70, and 100 kev. photon energies (with a few photons of 530 kev.). This isotope has a half life of approximately 47 hours and is thus impractical for clinical radiography. Its availability in desirable strength, however, permitted the relative evaluation of Gd^{153}, whose spectrum is almost identical (Fig. 1 *C*) and whose half life is 8 months. To date, Gd^{153} has been available only in small source strength and is impractical for other than the thinnest body sections. Yb^{169} (Fig. 1 *D*) with predominant photon energies of 52, 110, 190 and 310 kev. has proved to be the most practical. Its half life of 32 days affords a useful life of 3 to 4 months with presently available source strengths. Tm^{170} (Fig. 1 *E*), the subject of most previous investigations, exhibits photon energies of 52 and 84 kev. and also emits a continuous spectrum (Bremsstrahlung) up to 970 kev. as a result of beta particle absorption in the source material and its surroundings. The last spectrum shown, that of Lu^{177} (Fig. 1 *F*), exhibits high photon energies of 56, 110 and 210 kev. which result in poor contrast as discussed later in relation to Figure 3 *D*. Its short half life of 7 days also makes it impractical for clinical radiography.

Due to low source strengths and specific activities, Tm^{170} and Gd^{153} are unsuitable for chest radiography. A comparison was made of hand radiographs obtained using these sources with those obtained using Yb^{169}. In Figure 2, an Yb^{169} radiograph of the hand exposed at 0.75 second (*A*) is compared with a Gd^{153} radiograph (*B*) and a Tm^{170} radiograph (*C*). The longer exposure times necessary in using Gd^{153} and Tm^{170} are evident and their clinical imprac-

Table III

CHARACTERISTICS OF ISOTOPE SOURCES EVALUATED IN THIS STUDY

(to September 20, 1962)

Isotope	Approximate Half Life	Photon Energies (kev.)	Source Strength (2 mm. diameter×2 mm. length)	
			mrhm*	Remarks
Sm^{153}	2 da.	42, 70, 100, 530 (few)	600	Good
Gd^{153}	240 da.	42, 70, 100	10	Poor
Yb^{169}	32 da.	52, 110, 190, 310 (others)	2,000	Best
Tm^{170}	127 da.	52, 84, continuous spectrum to 970 (Bremsstrahlung)	100	Poor
Lu^{177}	7 da.	56, 110, 210	1,200	Good
Co^{60} (For comparison only)	5.3 yr.	1,170, 1,330	1,000	Good

* mrhm = milliroentgen per hour at one meter

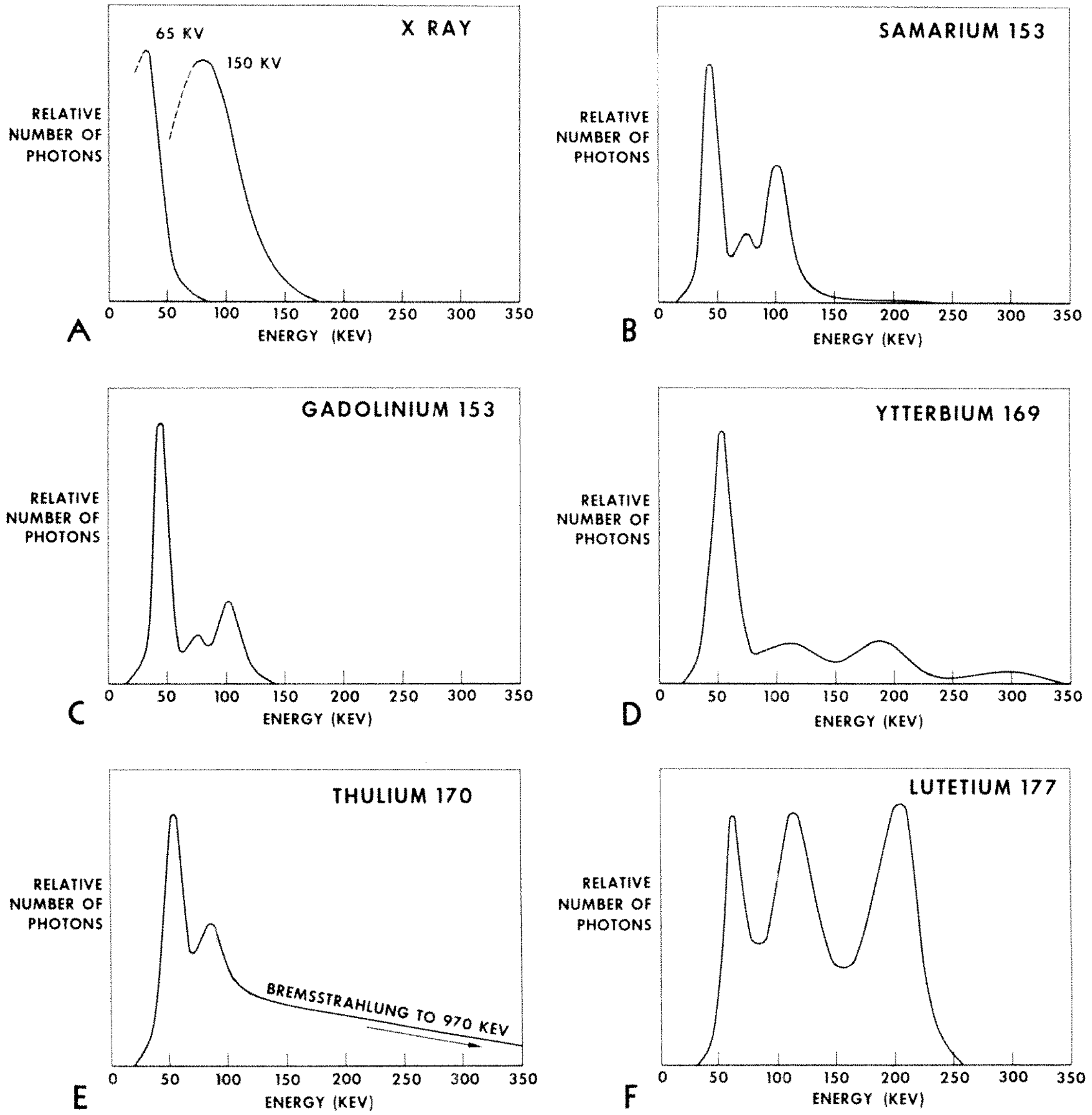


Fig. 1. Photon spectra of isotopes compared with x rays. (*A*) Continuous spectra of x-ray energies commonly used in roentgenography, 65 kv. and 150 kv. (*B*) Spectral distribution of photons from Sm^{153}. (*C*) Spectral distribution of photons from Gd^{153}. (*D*) Spectral distribution of photons from Yb^{169}. (*E*) Spectral distribution of photons from Tm^{170}. (*F*) Spectral distribution of photons from Lu^{177}.

ticality, unless higher source strengths become available, is obvious.

A conventional chest roentgenogram exposed with a 72 inch target film distance (TFD), 54 kv., 200 ma. and 1/20 second (*A*) is compared in Figure 3 with an Yb^{169} radiograph (*B*) of the same patient exposed 2 seconds, a Sm^{153} radiograph (*C*) exposed 10 seconds, and a Lu^{177} radiograph (*D*) exposed 3 seconds at 36 inches source film distance (SFD). The higher gamma energies in these isotopes, compared to the 54 kv. used for the chest roentgenogram, explain the lesser degree of contrast. The radiograph exposed with Sm^{153} gave the best contrast due to lower gamma energies, but unfortunately its half life of 47 hours prohibits its potential clinical use. The

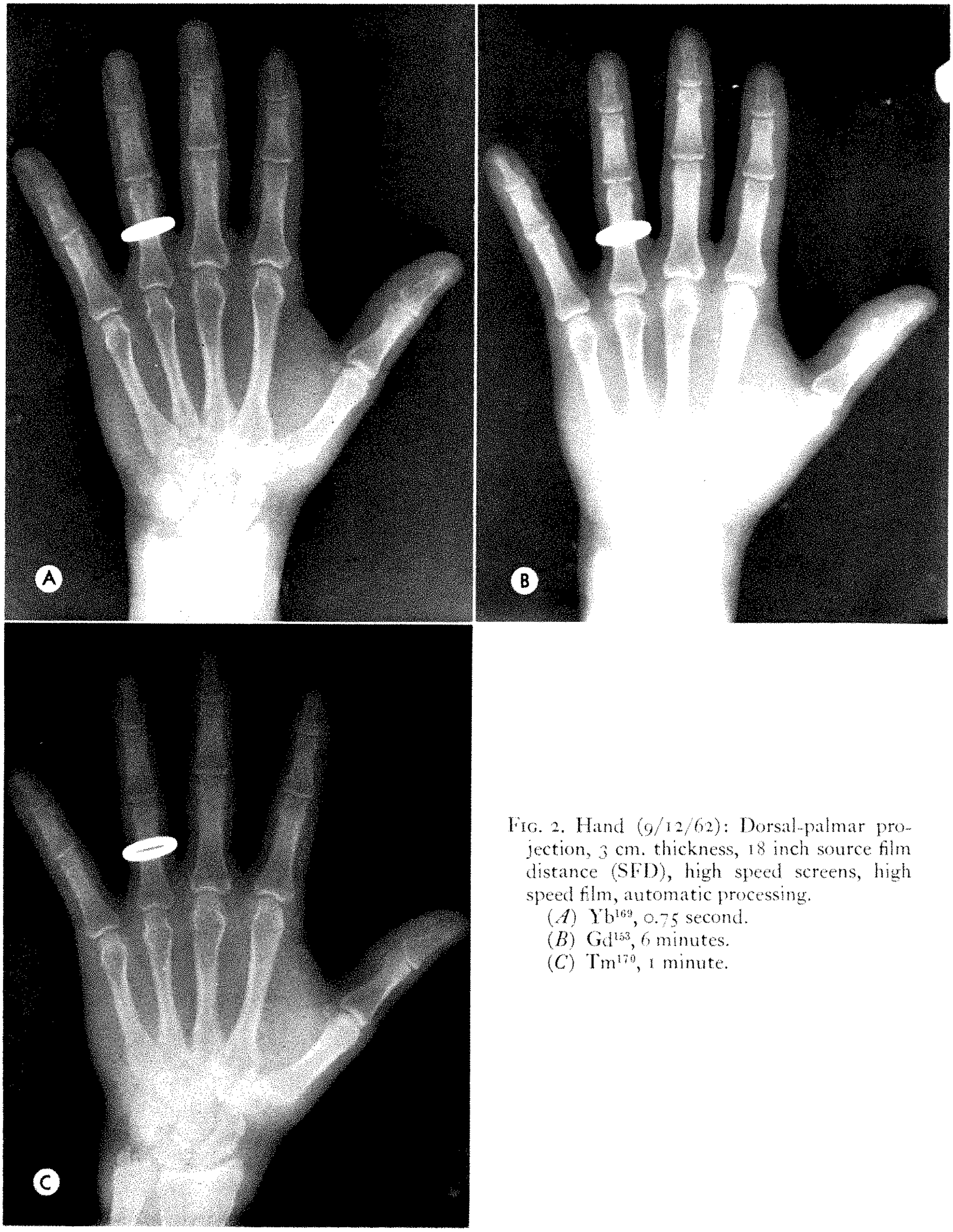


Fig. 2. Hand (9/12/62): Dorsal-palmar projection, 3 cm. thickness, 18 inch source film distance (SFD), high speed screens, high speed film, automatic processing.

(*A*) Yb^{169}, 0.75 second.
(*B*) Gd^{153}, 6 minutes.
(*C*) Tm^{170}, 1 minute.

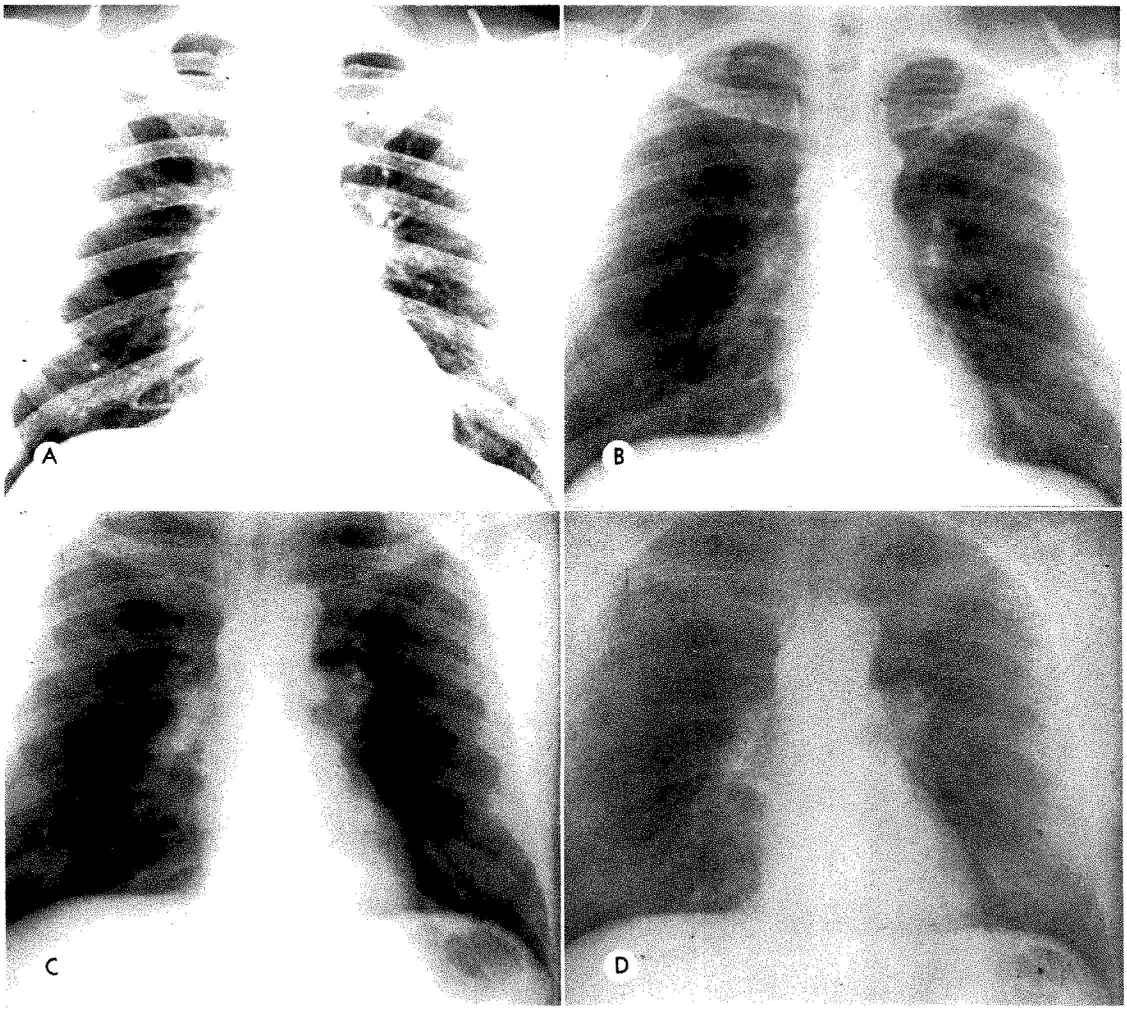


FIG. 3. Chest (5/2/62): Posteroanterior projection, 39 year old 175 pound patient, 23 cm. thickness. Histoplasmin positive, tuberculin negative. Multiple calcified parenchymal lesions and lymphadenopathy. High speed screens, high speed film, automatic processing.

(*A*) Roentgenogram—72″ target film distance (TFD), 54 kv., 200 ma., 1/20 second.
(*B*) Yb^{169} radiograph—36″ SFD, 2 seconds.
(*C*) Sm^{153} radiograph—36″ SFD, 10 seconds.
(*D*) Lu^{177} radiograph—36″ SFD, 3 seconds.

effect of the relatively higher energies of Lu^{177} is obvious when comparing this radiograph with those of Sm^{153} and Yb^{169}. The detail of pulmonary parenchymal structures in the Yb^{169} radiograph is quite acceptable for the purpose intended. The available source strength and energy spectrum of Yb^{169} are determining factors in evaluating this to be the most acceptable isotope for these purposes.

Data concerning typical exposures made with Yb^{169} sources are presented in Table IV, primarily to indicate the progress made in the development of an acceptable radiographic isotope source and to portray the relative degree of safety to both patient and operator with the use of such sources. The air skin dose is very small as compared to conventional roentgenographic techniques due to the emission of only a few discrete photon energies and the lack of low energy photons. A greater percentage of transmis-

Table IV

TYPICAL EXPOSURES WITH Yb^{169} SOURCES
(Royal Blue Film; High Speed Screens)

Body Part	Projection	Thickness (cm.)	Source to Film Distance (in.)	Air-Skin Dose[1] (mr)	Exposure (mrhm×sec.)[2]
Hand	DP	3	18	2	1,000
Ankle	Lat.	6	18	3	1,500
Leg	AP and Lat.	9	18	7	3,000
Leg (cast)	AP and Lat.	13	18	20	8,000
Pelvis	AP	25	36 (grid)	27	45,000
Skull	Lat.	16	36 (grid)	10	20,000
Chest	PA	22	36	2	2,100

[1] Air dose measured with center of Victoreen condenser r chamber at skin position without backscatter.

[2] mrhm source strength measured in milliroentgens per hour at one meter.

sibility of photons as compared with the x-ray beam results.[18]

The relation of air skin dose in milliroentgens to variable chest thickness for the three isotopes employed for chest radiography is presented in Figure 4. This shows that air skin dose is more a function of chest thickness than of the photon energies of various isotope sources.

The values of the product of source strength and exposure time (mrhm × seconds) obtained with numerous chest exposures using Yb^{169}, Sm^{153} and Lu^{177} are shown in Figure 5. Source strength is indicated in units of milliroentgens per hour at a meter because this measurement can be made readily by anyone with commonly available instruments which measure dose rate. Some previous investigators have used curies, intended to be an expression of disintegration rate, to represent source strength. Considerable confusion has thereby resulted because no instrument measures disintegration rate and accurate curie values are difficult to ascertain. A stated curie value assumes that all users concur on an identical decay scheme for the isotope and a method of measuring some ionizing

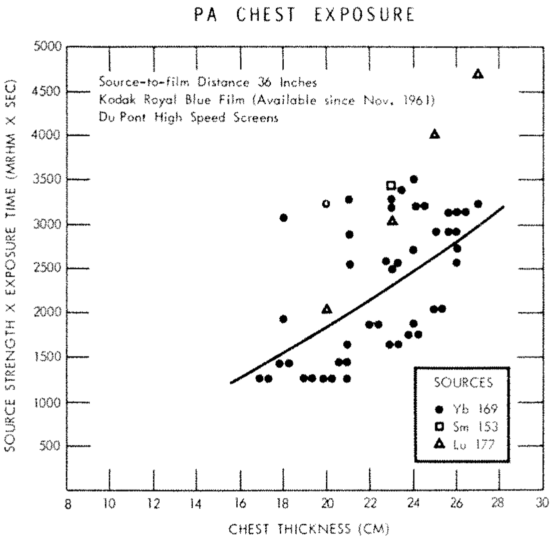


Fig. 5. Product of source strength and exposure time related to chest thickness for 3 isotope sources.

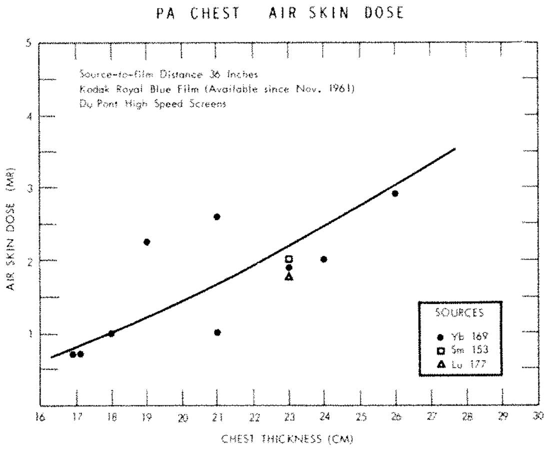


Fig. 4. Air skin dose for various chest thicknesses with 3 isotope sources. Dose is minimal.

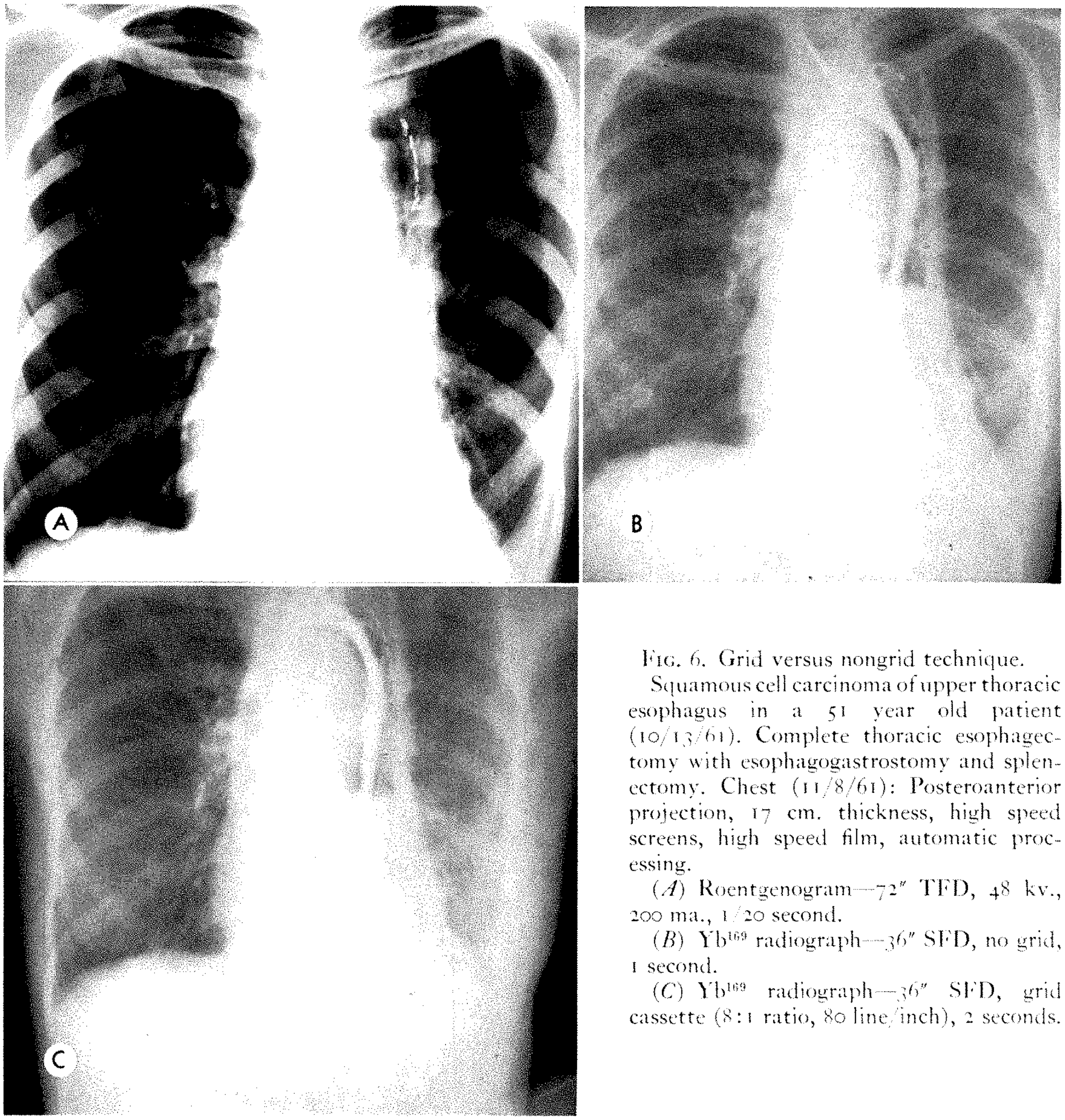


Fig. 6. Grid versus nongrid technique.

Squamous cell carcinoma of upper thoracic esophagus in a 51 year old patient (10/13/61). Complete thoracic esophagectomy with esophagogastrostomy and splenectomy. Chest (11/8/61): Posteroanterior projection, 17 cm. thickness, high speed screens, high speed film, automatic processing.

(*A*) Roentgenogram—72″ TFD, 48 kv., 200 ma., 1/20 second.

(*B*) Yb^{169} radiograph—36″ SFD, no grid, 1 second.

(*C*) Yb^{169} radiograph—36″ SFD, grid cassette (8:1 ratio, 80 line/inch), 2 seconds.

radiation indicated in the decay scheme. Actually, the decay scheme may not be accurately known for some years after the isotope has been used beneficially. The dose rate measured in mrhm for an isotope source with a given spectrum will probably remain an easily agreed upon and meaningful value.

The unit, *mrhm × seconds*, is chosen to denote exposure and permits the calculation of exposure times from such data as given in Figure 5. Exposure time for a given chest thickness is readily determined when source strength is known by dividing the exposure in mrhm × seconds by the source strength in mrhm.

EVALUATION OF TECHNICAL FACTORS

The high energy components of some of these isotopes logically suggested the use of *grids* to reduce secondary radiation for improvement of detail. Mayneord,[14] Has-

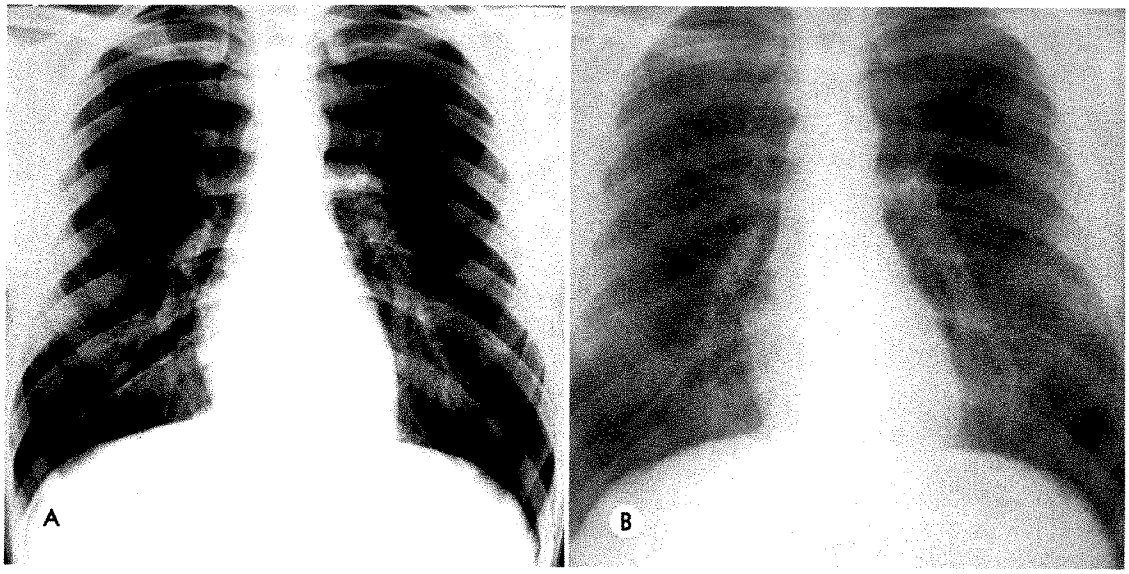


Fig. 7. Effect of long exposure time.
Normal chest (10/10/61): Posteroanterior projection of a 41 year old patient witth a chest of 19 cm. thickness, high speed screens, high speed film, automatic processing.
(*A*) Roentgenogram—72″ TFD, 48 kv., 200 ma., 1/20 second.
(*B*) Yb^{169} radiograph—36″ SFD, 25 seconds (source $3\frac{1}{2}$ half lives old).

terlik[9] and others have conducted such investigations with stationary and moving grids. We employed a grid cassette with an 8:1 ratio, 80 lines/inch, and, as described by Mayneord, found that a doubled exposure time was necessary. A comparison of an Yb^{169} chest radiograph exposed 1 second without a grid and 2 seconds with a grid at 36 inches source film distance (Fig. 6, *B* and *C*) was made with a chest roentgenogram exposed at 48 kv., 200 ma., 1/20 second at 72 inches target film distance (Fig. 6 *A*). Although a slight increase in detail was obtained by the use of a grid, it is believed that the required doubled exposure time renders the grid of doubtful value in achieving acceptable radiographic quality in chest radiography. Examination of the pelvis and skull, however, necessitates the use of a grid technique due to the thickness and density of these parts.

Rather *long exposure times* were used in the initial stages of this evaluation due to then available smaller source strengths. We discovered that once the fractional second exposure times employed in conventional roentgenography are exceeded, exceptionally long exposure times of 20, 30 and 40 seconds did not seriously further impair lung parenchymal detail. Yb^{169} chest radiographs can now be exposed in 1 second with most patients when the source is new and in no more than 8 seconds with a source three half lives old. A comparison is seen in Figure 7, *A* and *B* of a roentgenogram of the chest exposed 1/20 second and an Yb^{169} radiograph exposed 25 seconds with an early source which was $3\frac{1}{2}$ half lives old. The useful life of this isotope is therefore moderately satisfactory.

Reduction in source film distance to 36 inches for chest radiography proved justified after a comparison was made of radiographs exposed at 36 inches and 48 inches with chest roentgenograms at 72 inch target film distance. Little additional magnification at the shorter distance was seen and when compared with a teleroentgenogram the transverse diameter of the cardiac silhouette showed an increase of less than 1 cm. (Fig. 8, *A* and *B*).

Lead backed cassettes were employed throughout this study, supporting the observations of Hasterlik[9] in this regard.

CLINICAL COMPARISONS

Numerous clinical comparisons were carried out with radiographs, particularly of chest lesions, and conventional roentgenograms. In Figure 9 a roentgenogram demonstrating a tuberculous cavity in the left upper lobe (*A*) is compared with an Yb^{169} radiograph (*B*), made at a 36 inch source film distance and with an exposure time of 6 seconds (4,680 mrhm × sec.; source-strength 780 mrhm, air-skin dose 2.6 mr). The cavity in the left upper lobe is seen to good advantage in the isotope radiograph.

In Figure 10, a roentgenogram (*A*) and an Yb^{169} radiograph exposed 3 seconds (*B*) demonstrate a cavitating right upper lobe neoplasm. Similarly in Figure 11 a roentgenogram (*A*) and an Yb^{169} radiograph exposed 20 seconds (*B*) demonstrate an infected pneumatocele or abscess. In each of these instances the lesion can be recognized satisfactorily with isotope radiography.

Further studies have been made on thicker body sections, *i.e.*, the skull and pelvis. Both a reciprocating and stationary grid were used, the former giving better detail, but since its adaptation to portable use would be quite difficult, a stationary grid cassette was employed. Figure 12 is a skull radiograph exposed for 15 seconds at a 36 inch source film distance. Note the relative ease with which air containing structures can be recognized, a reflection of the higher energies of the Yb^{169} spectrum. Figure 13 is a portable Yb^{169} radiograph of the pelvis (1 minute exposure) made one day postoperatively following extensive reconstructive procedures on both hips.

Figure 14 shows comminuted fractures of the tibia and fibula as they are demonstrated on conventional roentgenograms (*A* and *C*) and on Yb^{169} radiographs exposed 10 seconds (*B* and *D*).

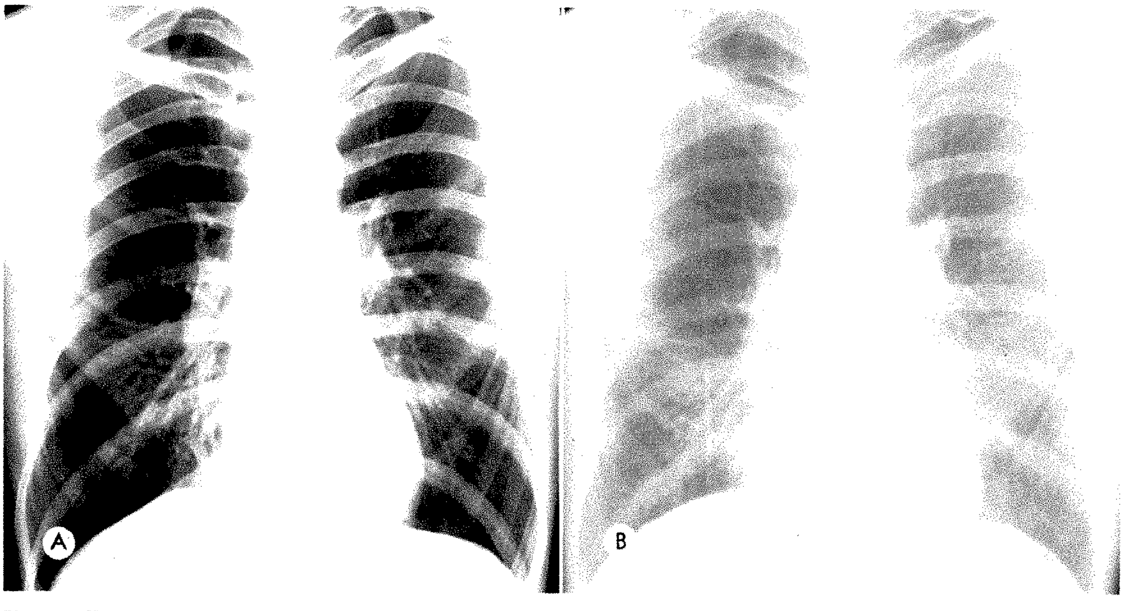


Fig. 8. Effect of short source film distance.

Normal chest. (10/20/61): Posteroanterior projection of a 23 year old patient with a chest of 21 cm. thickness, high speed screens, high speed film, automatic processing.

(*A*) Roentgenogram—72″ TFD, 52 kv., 200 ma., no grid, 1/20 second. Transverse diameter of cardiac silhouette is 12 cm.

(*B*) Yb^{169} radiograph—36″ SFD, no grid, 1 second.

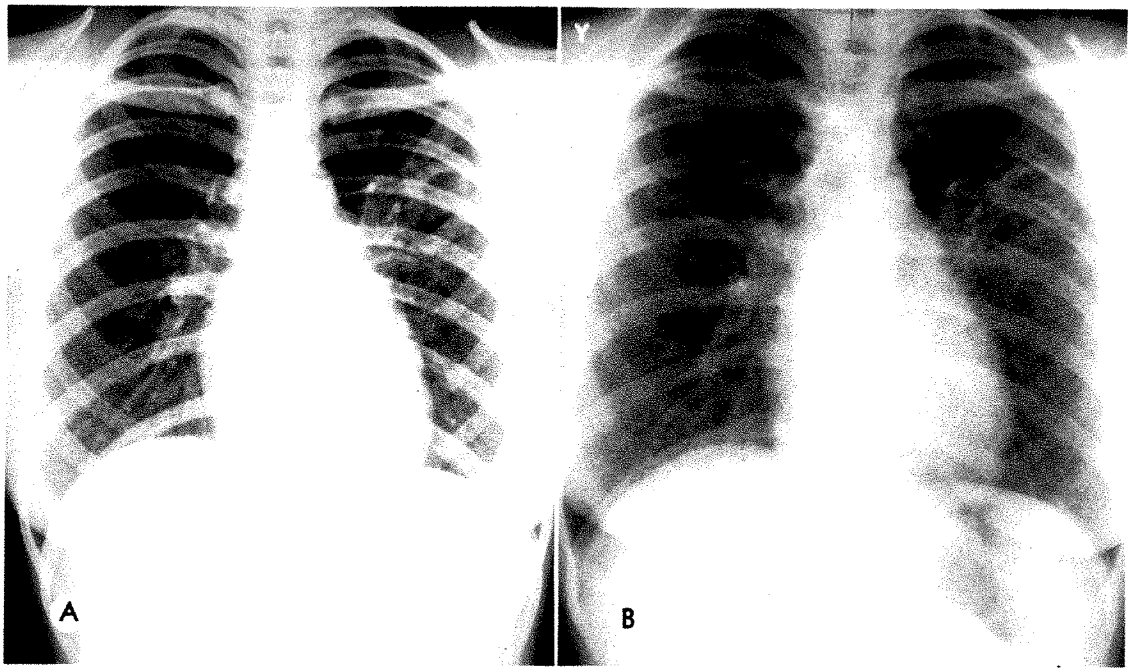


FIG. 9. An 18 year old patient with childhood tuberculosis in 1949. Last follow-up in 1960 was negative. Admitted to sanatorium in 1962. Sputum smear was positive for acid-fast organisms. Tubercle bacilli were cultured. Chest (6/5/62): Posteroanterior projection, 21 cm. thickness, high speed screens, high speed film, automatic processing.

(*A*) Roentgenogram—72″ TFD, 52 kv., 200 ma., no grid, 1/20 second. Moderately advanced tuberculosis with cavitation of left upper lobe.

(*B*) Yb^{169} radiograph—36″ SFD, no grid, 6 seconds.

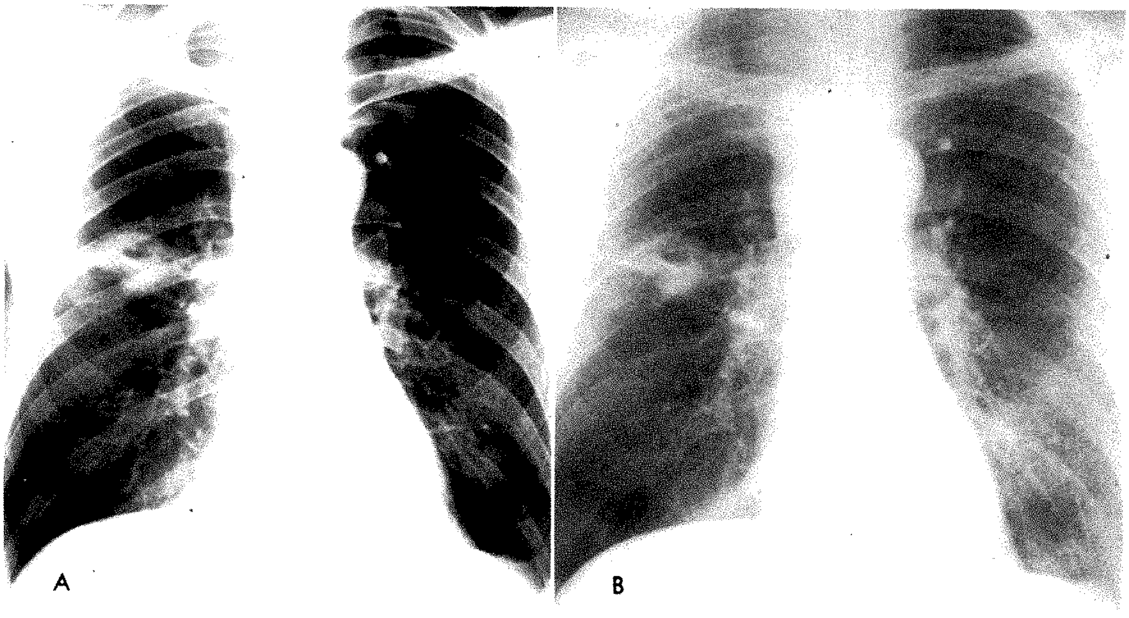


FIG. 10. Fifty-six year old patient with squamous cell carcinoma metastatic from lung (4/7/62). Biopsy of right cervical lymph node. Chest (5/21/62): Posteroanterior projection, 24 cm. thickness, high speed screens, high speed film, automatic processing.

(*A*) Roentgenogram—72″ TFD, 56 kv., 200 ma., no grid, 1/20 second. Cavitating bronchogenic neoplasm with peribronchial and peritracheal lymphadenopathy.

(*B*) Yb^{169} radiograph—36″ SFD, no grid, 3 seconds.

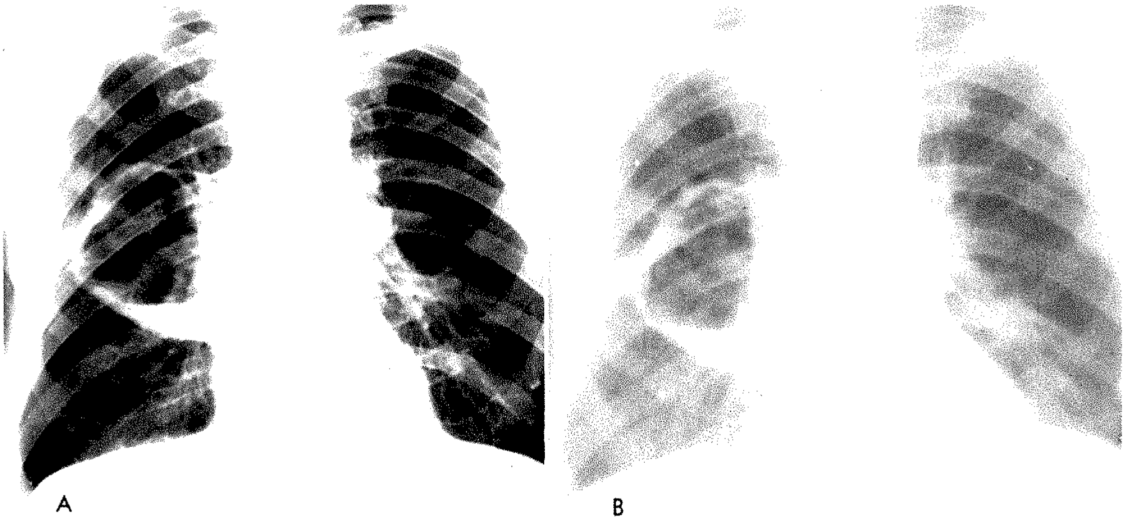


Fig. 11. Eighty-two year old patient with dysphagia attributed to neurogenic origin from cerebral thrombosis. On fifth hospital day hemoptysis was followed by slight temperature elevation. There were previous episodes of thrombophlebitis in legs. Chest (7/30/62): Posteroanterior projection, 26 cm. thickness, high speed screens, high speed film, automatic processing.

(*A*) Roentgenogram—72″ TFD, 58 kv., 200 ma., no grid, 1/20 second. Infected pneumatocele or abscess, secondary to pulmonary infarction.

(*B*) Yb^{169} radiograph—36″ SFD, no grid, 20 seconds.

DISCUSSION

It can be seen that radiography utilizing a portable radioactive Yb^{169} source proves this to be the most practical of those iso-

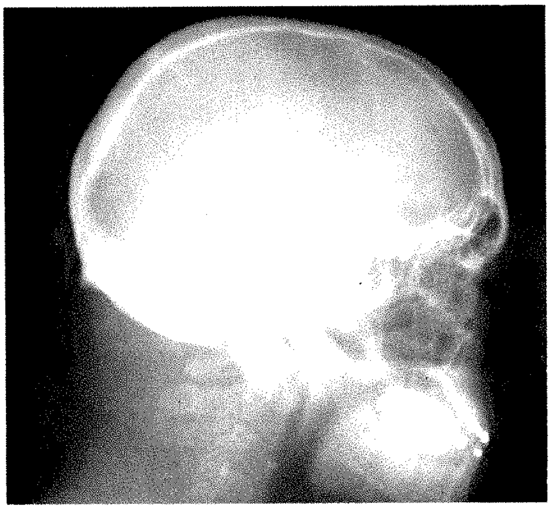


Fig. 12. Thirty-nine year old patient with a head thickness of 16 cm. Skull (9/12/62): Lateral projection, high speed screen, high speed film, automatic processing.

Yb^{169} radiograph—36″ SFD, grid cassette (8:1 ratio, 80 lines/inch), 15 seconds.

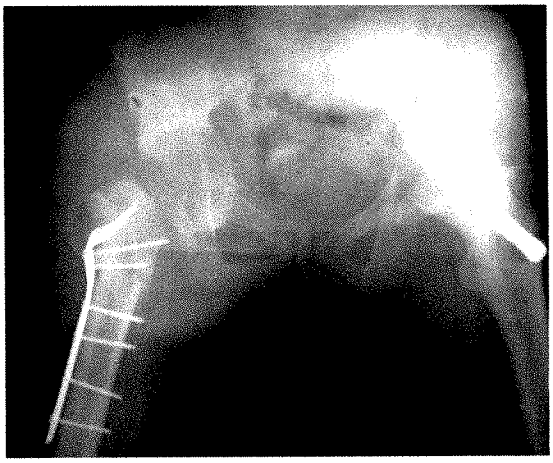


Fig. 13. Twenty-three year old patient with sickle cell disease (1956). Aseptic necrosis of both femoral and right humeral heads. (3/18,/59) Osteotomy and fusion of left hip; bone graft (metallic screw); insertion of Smith-Petersen nail. (5/9/60) Cup arthroplasty of right hip. (6/7/62) Osteotomy of right femoral head; removal of vitallium cup; Milch osteotomy with insertion of plate. Pelvis (6/8/62): Anteroposterior projection, bedside portable exposure, 24 cm. thickness, high speed screens, high speed film, automatic processing.

Yb^{169} radiograph—36″ SFD, grid cassette (8:1 ratio, 80 lines/inch), 1 minute. Note linear fracture of the right acetabulum.

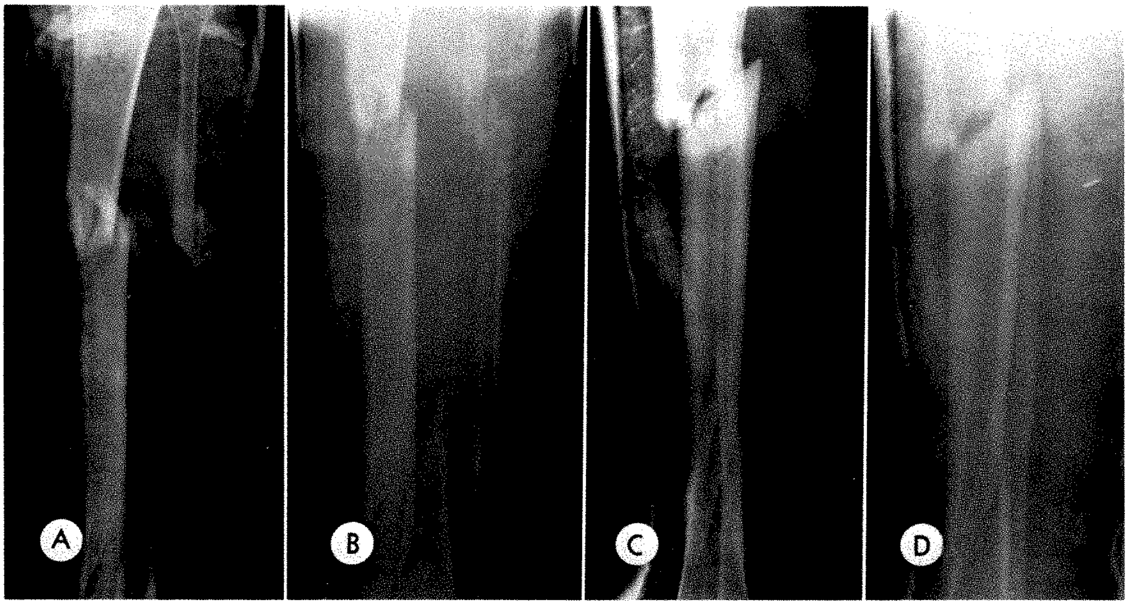


Fig. 14. Thirty-eight year old patient who sustained a compound fracture of right tibia when a 3,000 lb. die fell on leg. Debridement and open reduction was carried out with subsequent internal fixation (5/21/62). Leg (6/5/62): Comminuted, compound fractures of proximal tibia and fibula, oblique fracture distal to tibial shaft. Plaster cast.

(*A*) Anteroposterior roentgenogram—36″ TFD, 42 kv., 100 ma., no grid, 3/20 second.
(*B*) Yb^{169} radiograph—18″ SFD, no grid, 10 seconds.
(*C*) Lateral roentgenogram—same factors as in *A*.
(*D*) Yb^{169} radiograph—same factors as in *B*.

topes evaluated. It has a reasonably acceptable half life of 32 days and a useful life of about 3 to 4 months (3 to 4 half lives.) Due to some high energy photons in its gamma spectrum, radiographic contrast is somewhat less pronounced than that obtained with conventional roentgenography. The use of a grid proved necessary in the examination of thick body sections such as the skull and pelvis but offered little advantage in the examination of the extremities or chest.

The advantages of portable radioactive sources for radiography in remote areas, in disaster situations, in the operating room, in the hospital room (Fig. 15, *A*, *B* and *C;* and 16, *A* and *B*) and in the patient's residence are obvious due to source flexibility and adaptability. This method is still in the developmental phase and sources of smaller size, higher specific activity and longer half life may be desired; however, radiography of useful and acceptable quality under the circumstances described can now be obtained by using Yb^{169} as a source.

Radiation protection of personnel is effectively achieved by adequate shielding in the exposure unit for transportation and storage. The air skin dose to the patient is very low as shown in Table IV and Figure 4. Backscatter radiation to the operator is low (1) due to small total beam dose resulting from a greater percentage of transmissibility of the beam because of absence of very low photon energies and (2) due to narrow collimation of the beam.

CONCLUSIONS

Radiography using portable radioactive isotope sources with the principal advantages of easy portability and independence from electrical power has been evaluated. Optimization of technical factors in relation to screens and films is necessary. Very low doses to the patient were calculated and confirmed by measurement. This

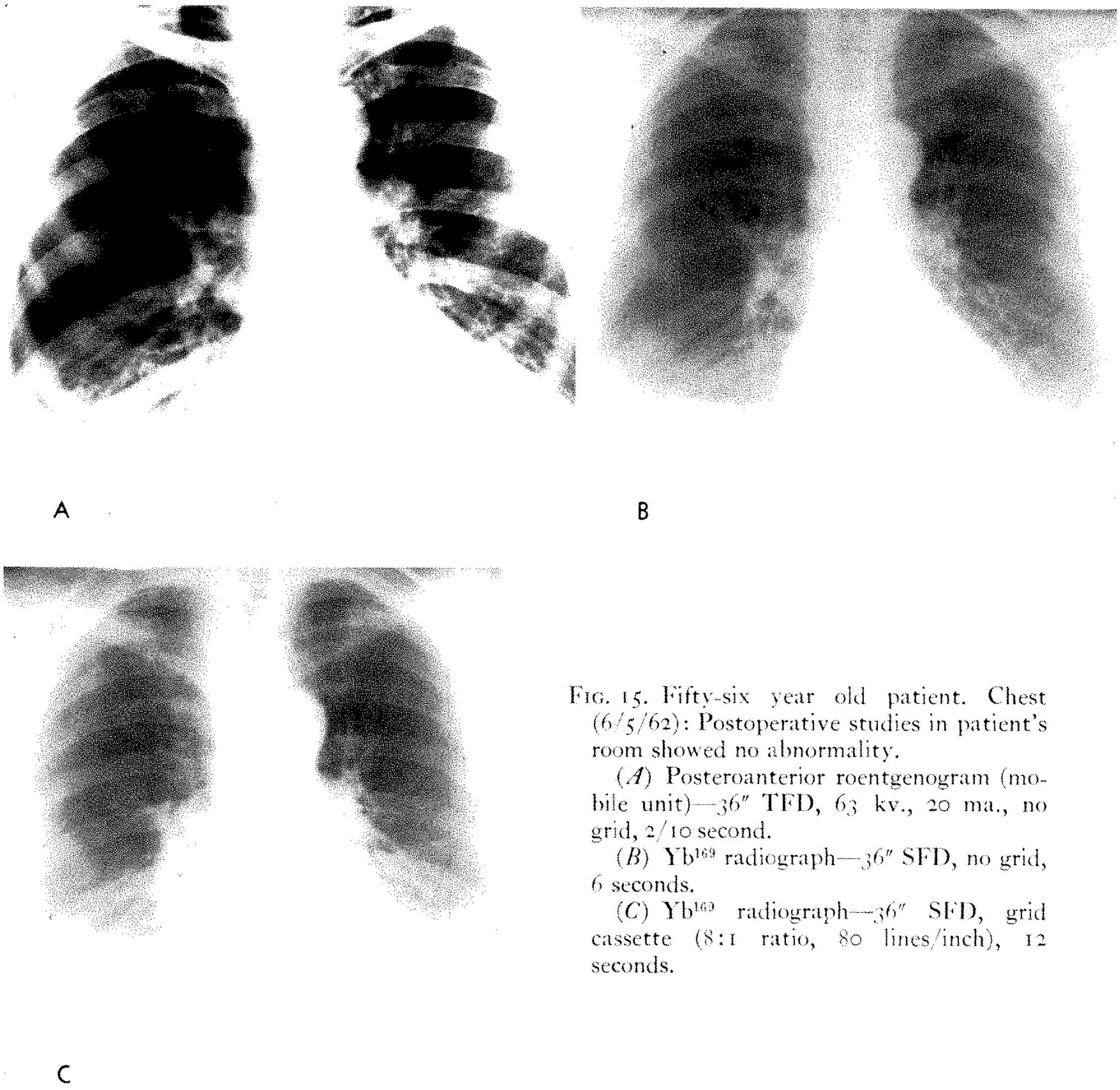
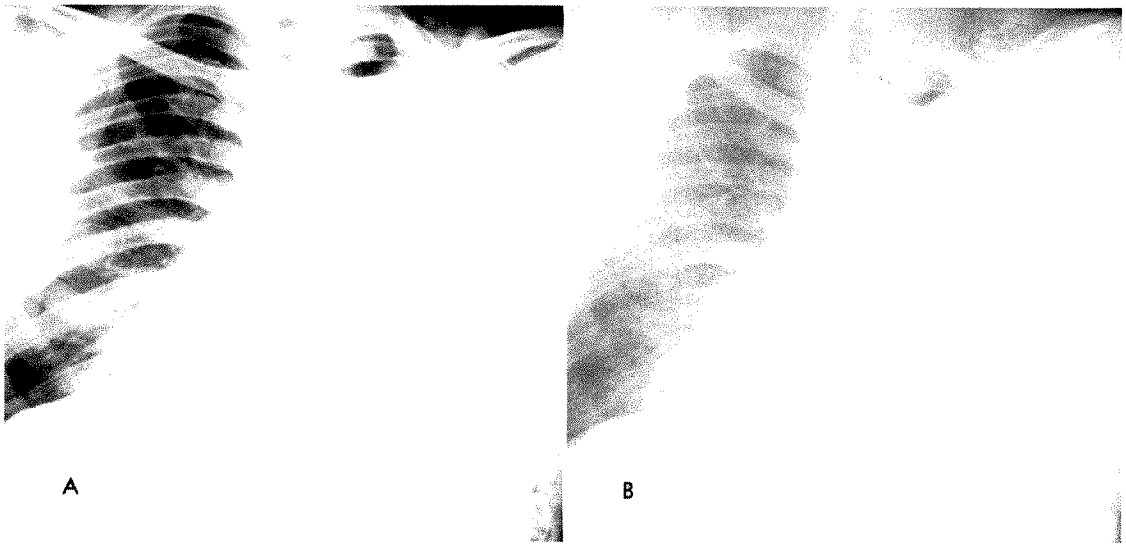


FIG. 15. Fifty-six year old patient. Chest (6/5/62): Postoperative studies in patient's room showed no abnormality.

(*A*) Posteroanterior roentgenogram (mobile unit)—36″ TFD, 63 kv., 20 ma., no grid, 2/10 second.

(*B*) Yb^{169} radiograph—36″ SFD, no grid, 6 seconds.

(*C*) Yb^{169} radiograph—36″ SFD, grid cassette (8:1 ratio, 80 lines/inch), 12 seconds.



technique does not compete with conventional roentgenography in fixed installations with adequate electrical power. Yb^{169} has proved to be the most practical of the isotopes evaluated to date.

The advantages of portable isotope radiography in remote areas, disaster and other portable applications are many. This technique has reached the stage of clinical diagnostic usefulness.

Kenneth L. Krabbenhoft, M.D.
Harper Hospital
Detroit 1, Michigan

REFERENCES

1. Beronius, P., Forberg, S., Henrikson, C. O., and Söremark, R. Use of iodine-125 as x-ray source in roentgen diagnostics. *International Journal of Applied Radiation and Isotopes*, 1962, *13*, 253–254.
2. Burke, D. E. Isotope radiographs for localization of renal calculi during surgery: new truly portable radiographic unit using radioisotope (thulium 170) as energy source. *J. Urol.*, 1956, *76*, 508–519.
3. Coleman, E. W. Portable thulium 170 x-ray unit. Proceedings of Health Physics Society, June 25–27, 1956, 8–14.
4. Dennis, G. E., and DeLuca, H. A. Use of radioactive isotopes for diagnostic radiology. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1954, *72*, 661–665.
5. Green, F. L. Low energy photon emission from radioisotopes. *Transactions of American Nuclear Society*, 1962, *5*, 207.
6. Green, F. L. Unpublished data, 1959.
7. Green, F. L., and Cheek, W. D. New low energy photon sources for industrial radiography. *Proceedings of International Conference on Peaceful Uses of Atomic Energy*, 1958, *19*, 169–175.
8. Green, F. L., Disney, C. T., Cheek, W. D., and Graham, G. P. Radiation characteristics of a Sm^{153} photon source. *Transactions of American Nuclear Society*, 1958, *1*, 66–67.
9. Hasterlik, R. J. Portable thulium x-ray unit. III. Clinical radiography with a Tm^{170} source. *Nucleonics*, 1954, *12*, 37.
10. Ireland, H. J. D. Radiography with radioactive isotopes. *Practitioner*, 1957, *178*, 447–453.
11. Krebs, A. T., and Kereiakes, J. G. Portable isotopic radiographic units. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1956, *76*, 168–175.
12. Lange, W. H., Greene, J. L., Green, F. L., and Graham, G. P. Advances in isotope radiography. *X-ray Technician*, 1963, *34*, 197–206.
13. Mayneord, W. V. Radiography of human body with radioactive isotopes. *Lancet*, 1952, No. 262, 276–278.
14. Mayneord, W. V. Radiography of human body with radioactive isotopes. *Brit. J. Radiol.*, 1952, *25*, 517–525.
15. Mayneord, W. V., and Ireland, H. J. D. Radiography with thulium 170 and xenon 133. *Brit. J. Radiol.*, 1956, *29*, 277–285.
16. Myers, W. G. On a new source of x-rays. *Ohio M. J.*, 1962, *58*, 772–773.
17. Nurnberger, C. E. Medical radiography with radioactive sources (Samarium^{153}). Unpublished data, 1960.
18. Nurnberger, C. E. Medical radiography with gamma rays of radioactive sources (Ytterbium^{169}). Unpublished data, 1961.
19. Roberts, J. E. Gamma-radiograph. *Brit. J. Radiol.*, 1956, *29*, 629.
20. Shemesh, A., and Rice, W. E. Application of film intensification to radioisotopic radiography. Army Medical Research Laboratory Report, Fort Knox, Kentucky, 1956, No. 219, 1–16.
21. Sinclair, W. K., and Smith, B. J. Possibility of using thulium 170 as teleradiographic source for localization purposes in teletherapy with cobalt 60. *Radiology*, 1956, *66*, 104.
22. Spangenberg, H. D., Jr. Production of roentgenograms by means of x-ray radiation from artificially radioactive isotopes. Ohio State Univ. Eng. Expt. Sta. News, 1948, *20*, No. 5, 48–50.
23. Spangenberg, H. D., Jr., and Pool, M. L. Production of roentgenograms by x-ray radiations obtained from radioactive x-ray emitters. *J. Am. Dent. A.*, 1953, *47*, 624–630.
24. Spangenberg, H. D., Jr., and Pool, M. L. Production of clinical roentgenograms by

---

←

Fig. 16. Thirty-nine year old patient. Chest (6/7/62): Postoperative studies were carried on in patient's room. Patient underwent pneumonectomy on the preceding day.
(*A*) Posteroanterior roentgenogram (mobile unit)—38″ TFD, 63 kv., 20 ma., 3/10 second.
(*B*) Yb^{169} radiograph—36″ SFD, no grid, 6 seconds.

means of compact radioactive x-ray and gamma-ray sources. Ohio State Univ. Research Foundation, R.F. Project 610, Columbus 10, Ohio, 1957, 1–29.

25. UNTERMYER, S. Portable thulium x-ray unit: I. Portable unit. *Nucleonics*, 1954, *12*, 35–36.

26. WEST, R. Low-energy gamma-ray sources. *Nucleonics*, 1953, *11*, 20–23.

27. ZODIEV, V. V., DMOKHOVSKII, V. V., and MASLOV, L. A. Radiography with aid of thulium preparation. *Vestn. Rentgenol. Radiol.*, 1960, *35*, 62–67.

* * *

NORMAL AND PATHOLOGIC ROENTGEN ANATOMY OF THE MIDDLE EAR AND MASTOID PROCESS*

By LEWIS E. ETTER M.D.,† *and* LAWRENCE C. CROSS, R.T.‡
PITTSBURGH, PENNSYLVANIA

SINCE the availability of antimicrobial medications, the incidence of disease involving the middle ear and mastoid process coming to the attention of the radiologist has been greatly reduced. It is now quite unusual to see a patient who has acute mastoiditis, but not so uncommon to be called upon to make examinations of persons who have symptoms such as dizziness, nausea, tinnitus and foul drainage from the ear, especially in some of the older age group who have had ear disease before the advent of the antibiotic era. Most of the work of the radiologist, then, will be concerned with examination of the middle ear and mastoid process for evidence of changes which have been progressing over a long period of time and which may require otologic surgical intervention for correction. The question before us is usually, "What does the otologic surgeon want us to tell him?"

METHODS OF EXAMINATION

An adequate conventional study of the middle ear and mastoid process should include a Schüller view instead of the formerly popular Law projection, a Stenvers' view which will include the mastoid tips and make unnecessary anteroposterior projections for them, the Chamberlain-Towne projection, the Mayer axial projection and Owen's modification of it with, in addition, a basal view of the skull. Each of these positions will be discussed individually with an explanation of the normal roentgen anatomy and followed by some examples of pathologic alterations.

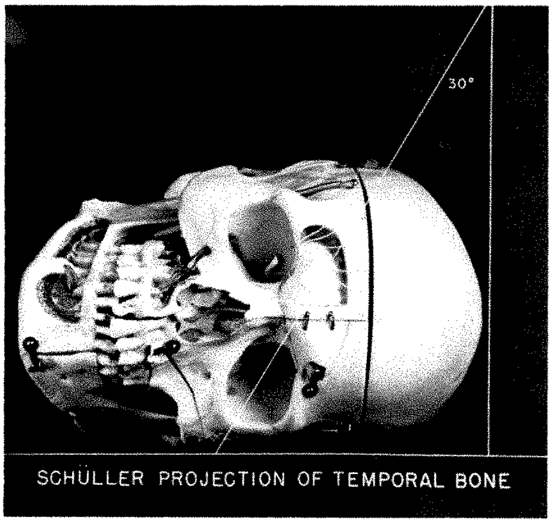


Fig. 1. Skull positioned for Schüller's projection as viewed from the front.

SCHÜLLER'S PROJECTION

Figures 1 and 2 show the position of the skull for Schüller's projection as viewed from the front (Fig. 1) and from above (Fig. 2). The position of the patient on the examining table for this study is shown in Figure 3, which requires only a single 30 degree angle towards the feet and is much simpler than the Law projection requiring two 15 degree angles, and therefore less likely to be accurate and reproducible. This projection is also practically identical to the Runström projection described by the Swedish authors for this lateral oblique position. Figure 4 made in the Schüller projection shows the middle ear and mastoid process with the various features designated. This view, along with the Owen's

---

* Presented at the Sixty-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 2-5, 1962.
A Grant from the Health Research and Services Foundation of Pittsburgh to carry on this research is gratefully acknowledged.
† Western Psychiatric Institute and The Falk Clinic, School of Medicine, University of Pittsburgh.
‡ Research X-ray Technician, Western Psychiatric Institute.

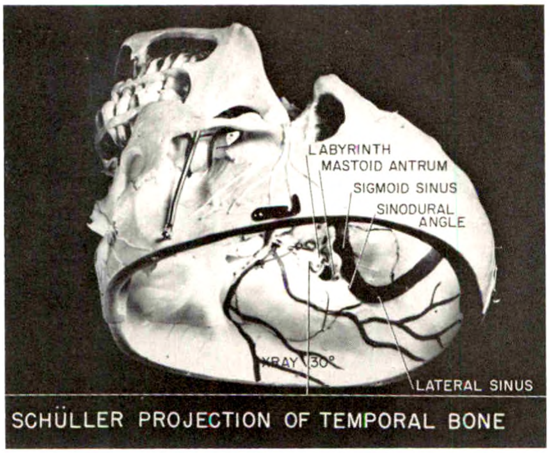


Fig. 2. Skull positioned for Schüller's projection as viewed from above.

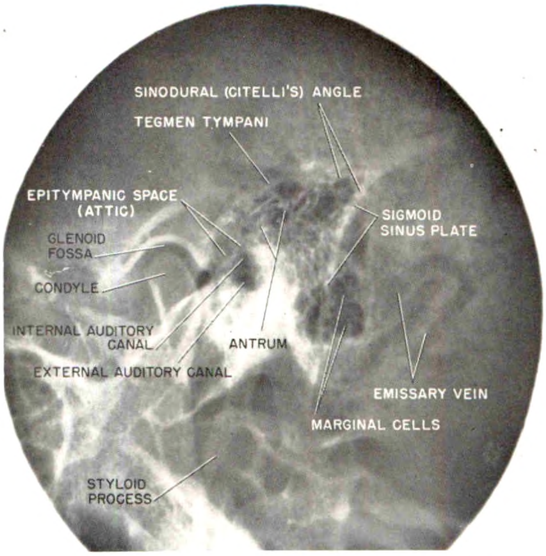


Fig. 4. Roentgenogram made in Schüller's projection.

modification of the Mayer view, is quite useful in showing changes in the epitympanic space (attic) and the sinodural angle of Citelli.

STENVERS' PROJECTION

Figures 5 and 6 are Stenvers' views showing the position of the skull from above (Fig. 5) and from the side (Fig. 6). The mastoid tips and an excellent profile of the petrous ridge, especially of the internal acoustic meatus, the otic capsule with

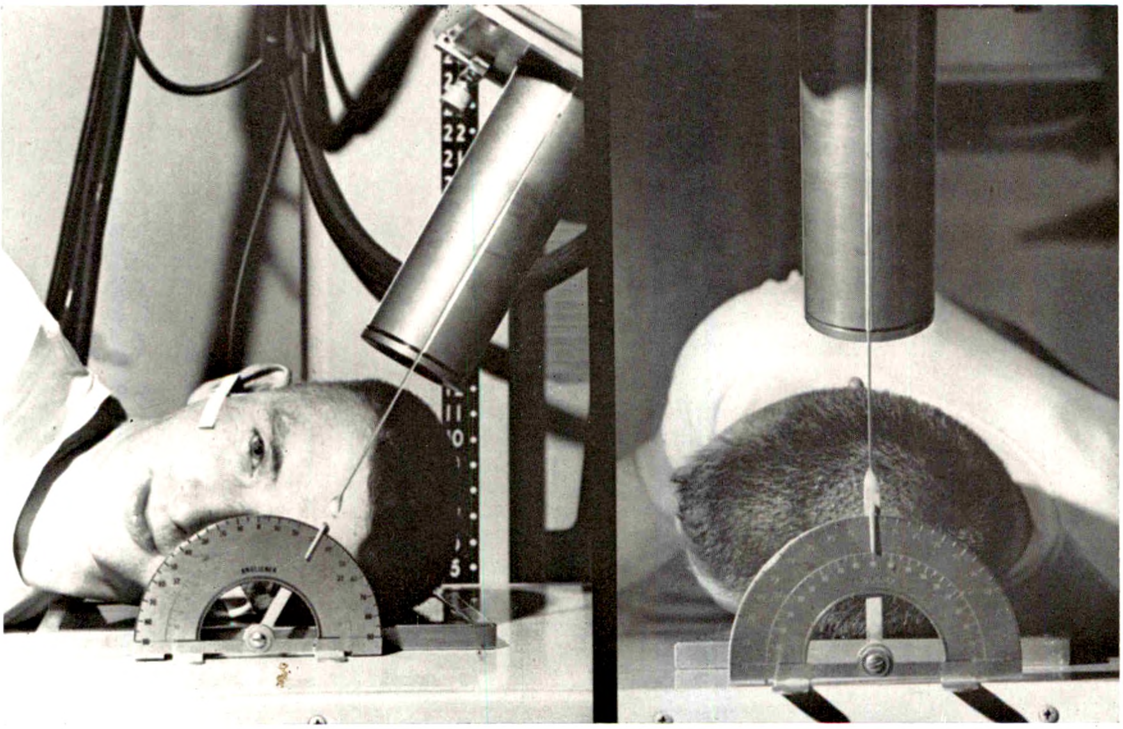


Fig. 3. Patient positioned for Schüller's projection.

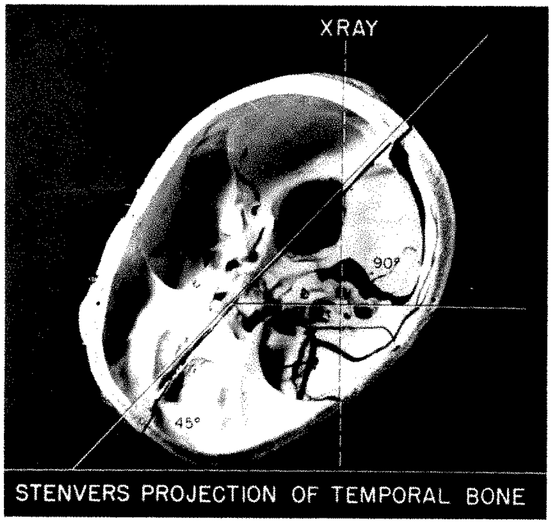


Fig. 5. Skull positioned for Stenvers' projection from above.

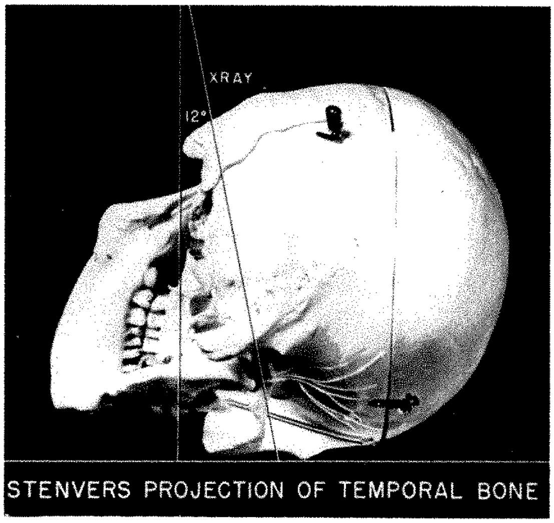


Fig. 6. Skull positioned for Stenvers' projection from the side.

labyrinth, and the mastoid antrum just lateral to these structures are also demonstrated on these studies. In Figure 7 the positioning of the patient is shown. Figure 8 illustrates the anatomy of the ear as seen roentgenographically in the Stenvers' position.

CHAMBERLAIN-TOWNE'S PROJECTION

With regard to the anteroposterior oblique or the Chamberlain-Towne projection

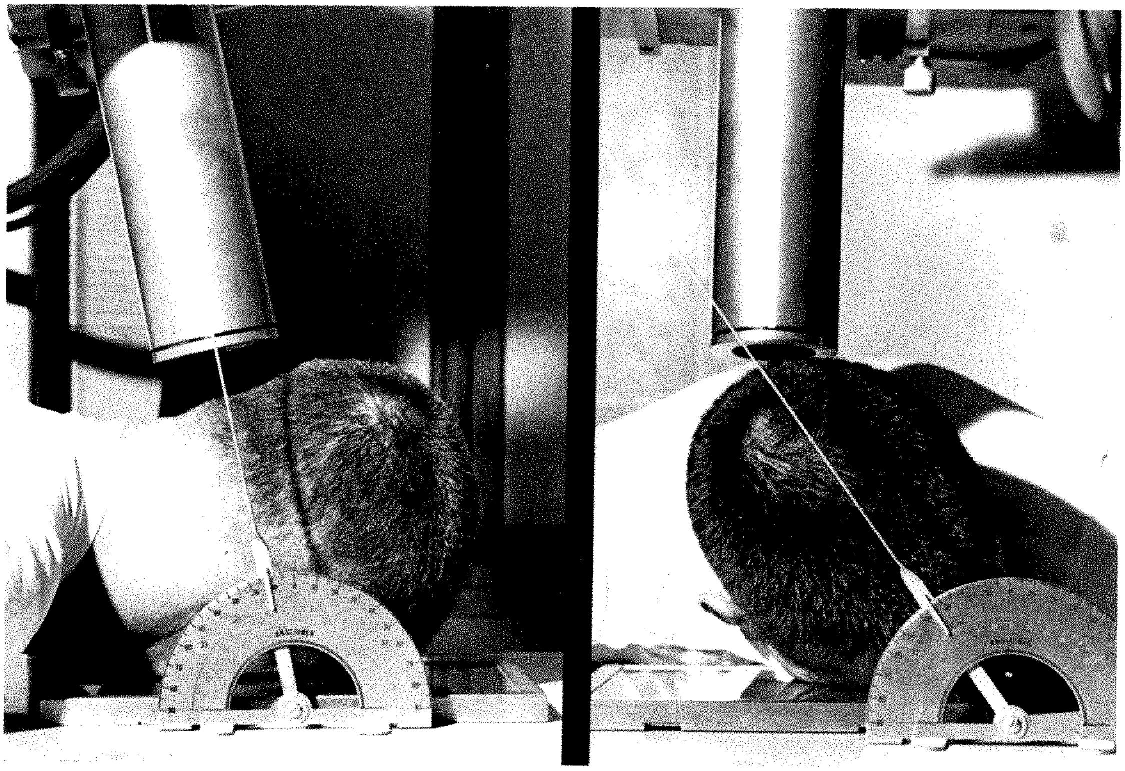


Fig. 7. Patient positioned for Stenvers' projection.

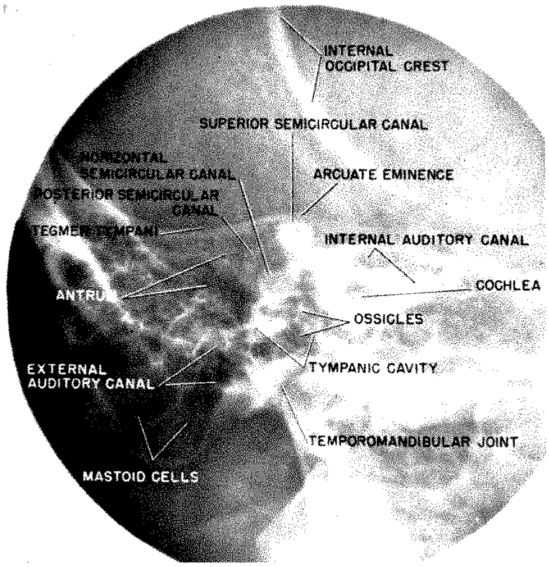


FIG. 8. Roentgenogram made in Stenvers' projection.

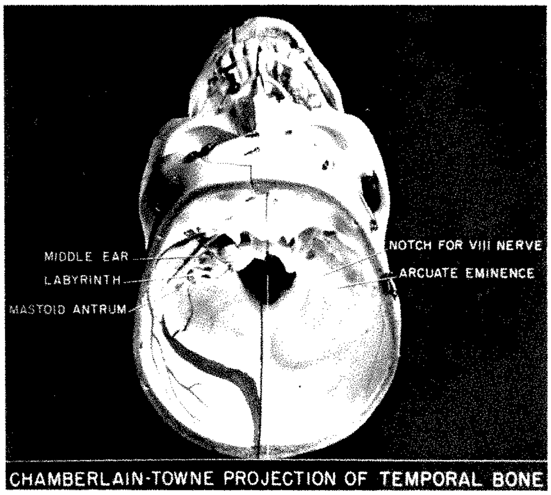


FIG. 9. Skull positioned for Chamberlain-Towne projection.

(Fig. 9), we have found it much more satisfactory to roentgenograph the two sides separately using a very small cylinder (Fig. 10) because much better definition of the structures in the middle ear and the petrous ridge is obtained. The angle may be varied (30–40 degrees) but the structures are usually demonstrated from side to side on the roentgenogram (Fig. 11). This is one of the most important complementary exami-

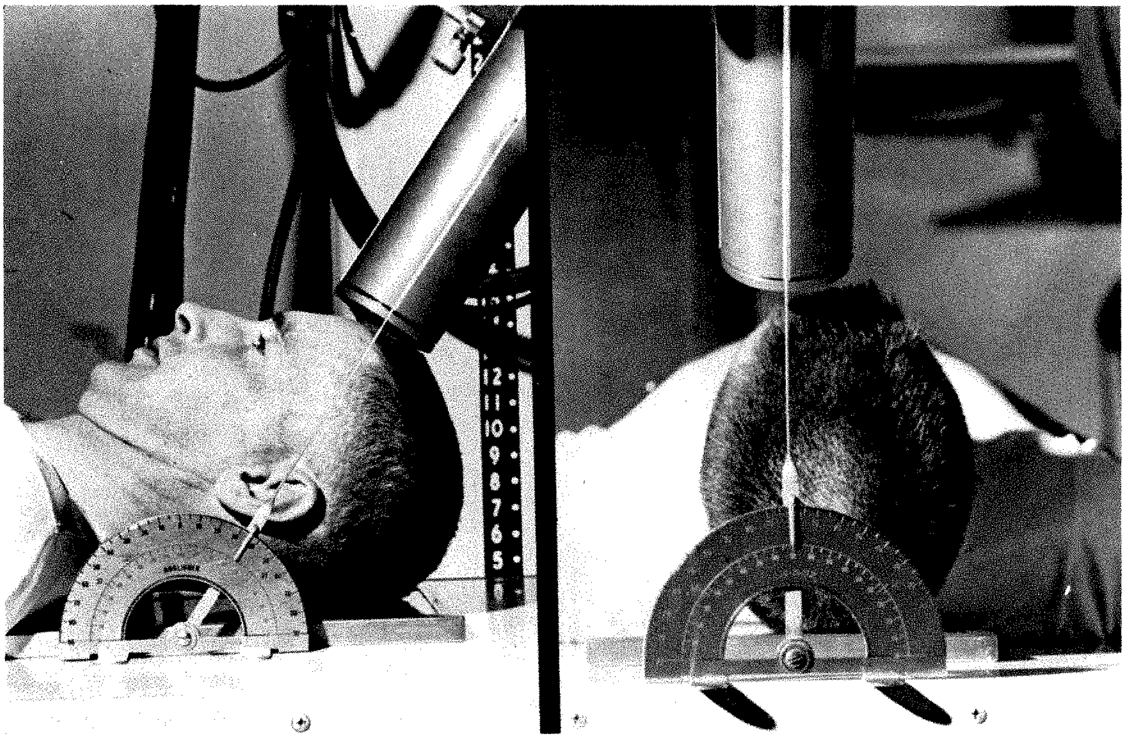


FIG. 10. Patient positioned for Chamberlain-Towne projection.

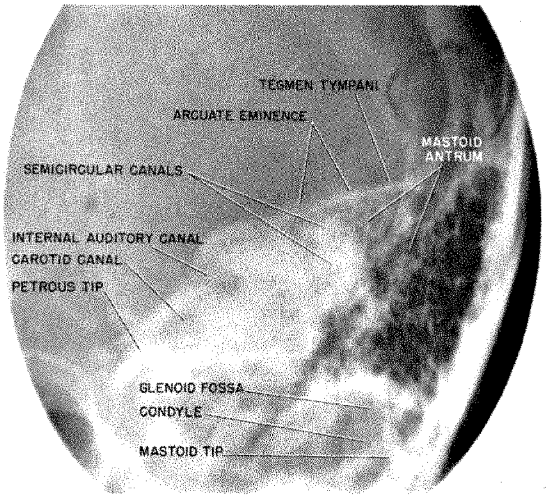


Fig. 11. Roentgenogram made in Chamberlain-Towne projection.

nations to be made, especially for a comparison with the Stenvers and Mayer projections in the evaluation of the mastoid antrum.

MAYER'S AXIAL PROJECTION

The Mayer axial view of the petrous ridge devised in Vienna many years ago is particularly good for the delineation of the tympanic cavity, the bony bridge, the aditus, the epitympanic space (attic) and the mastoid antrum. For this position (Fig. 12) the skull is placed at a ventro-dorsal angle of 45 degrees from the table-top and the central ray is directed caudad at a cephalo-caudal angle of 45 degrees (Fig. 13). The patient positioned on the examining table for this view is shown in Figure 14 and the resulting roentgenogram with the demonstration of the various roentgen features is shown in Figure 15. A conventional 45-45 degree angle is not necessary for optimal visualization of the tympanic cavity; a cephalo-caudal angle of 45 degrees with approximately a 35 degree ventro-dorsal angle has proved more satisfactory (Fig. 16). Often one must vary the ventro-dorsal angle from side to side on the same person, sometimes as low as 20 degrees in order to obtain optimal visualization of the middle ear cavity; otherwise, it may be obscured by the mastoid process.

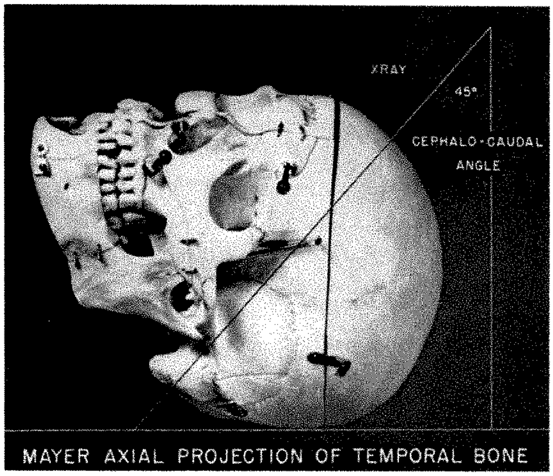


Fig. 12. Skull positioned for Mayer's axial projection.

OWEN'S MODIFICATION OF THE MAYER PROJECTION

Owen modified Mayer's projection by using a double 30 degree angle: a 30 degree cephalo-caudal and a 30 degree ventro-dorsal angle, which gives a somewhat foreshortened view of the same structures visualized in the Mayer projection. The skull as viewed from in front in this modified projection is shown in Figure 17 and from above in Figure 18. The positioning of the patient on the table is shown in Figure 19. The resulting roentgenogram (Fig. 20) gives an excellent view from the standpoint

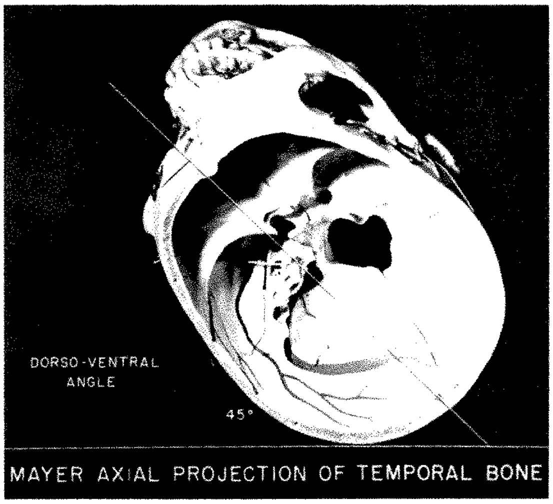


Fig. 13. Angle of central ray in Mayer's axial projection.

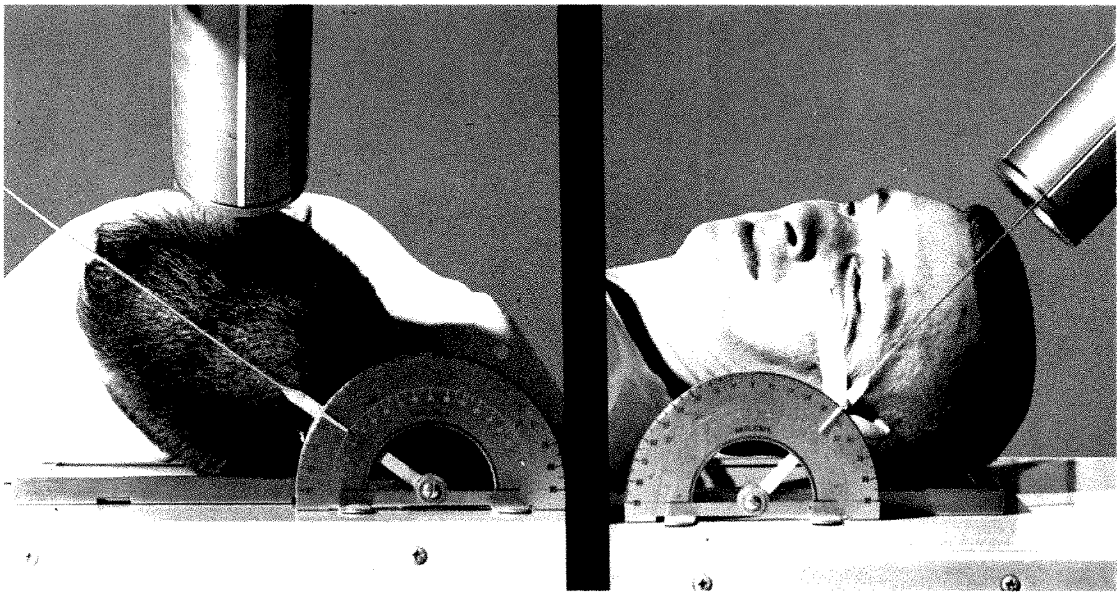


Fig. 14. Patient positioned for Mayer's axial projection.

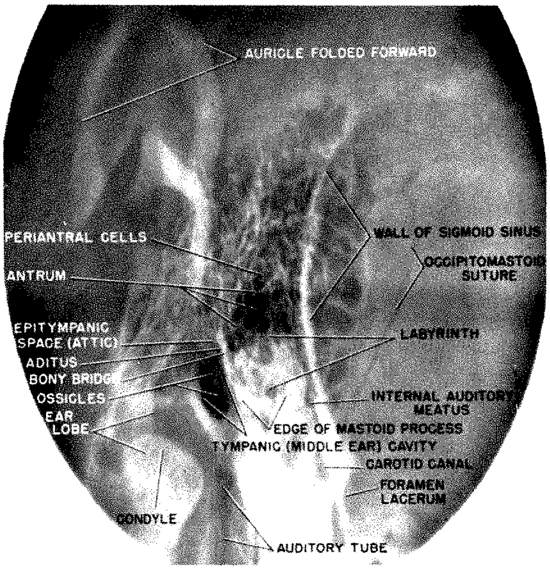


Fig. 15. Roentgenogram made in Mayer's axial projection.

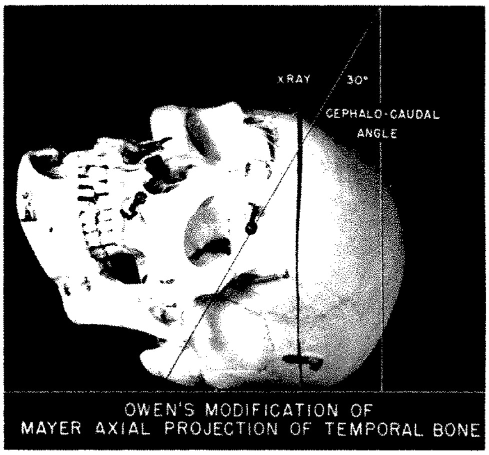


Fig. 17. Skull positioned for Owen's modification of Mayer's axial projection from in front.

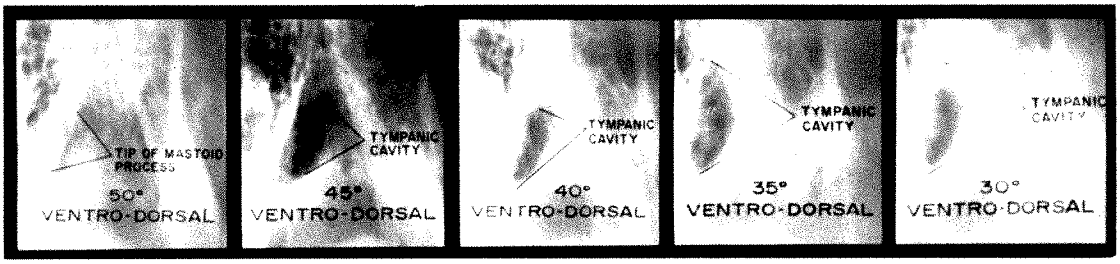


Fig. 16. Roentgenograms showing variations of the ventro-dorsal angle in Mayer's axial projection.

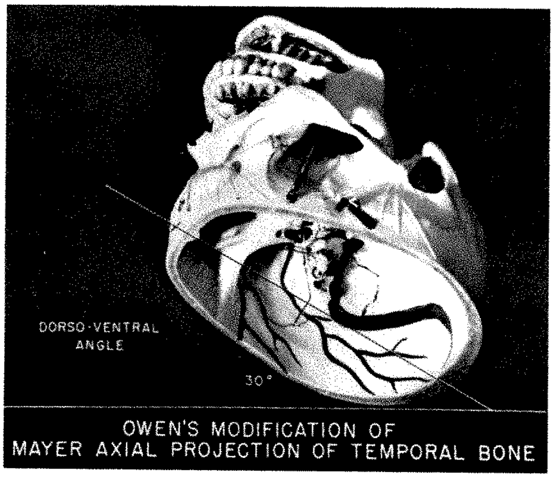

DORSO-VENTRAL ANGLE
30°
OWEN'S MODIFICATION OF MAYER AXIAL PROJECTION OF TEMPORAL BONE

Fig. 18. Skull positioned for Owen's modification of Mayer's axial projection from above.

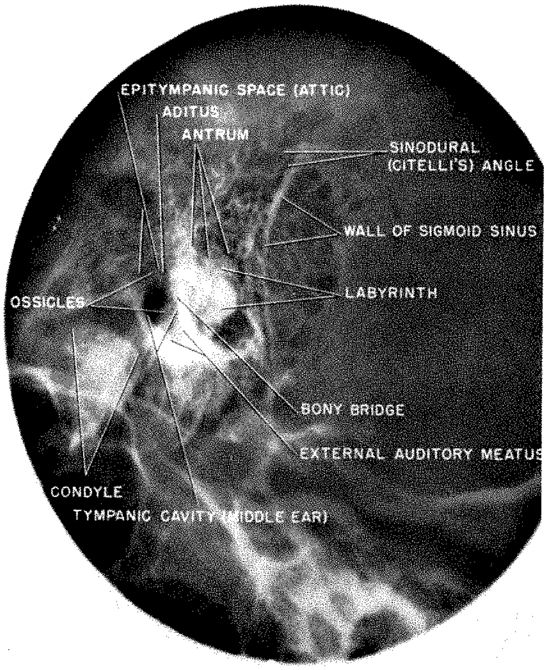


Fig. 20. Roentgenogram made in the Owen's modified Mayer axial position.

of the otologic surgeon since it more nearly approximates what he sees at surgery than any of the other views.

BASAL PROJECTION

Finally, the use of the basal projection, either vertico-submental or submento-vertical, depending upon the degree of mobility of the patient's neck, is recommended. Here, as in the Towne view (Fig. 21), each side is done separately with as small a cylinder as possible. The angles are varied as indicated (Fig. 22). Figure 23 shows that

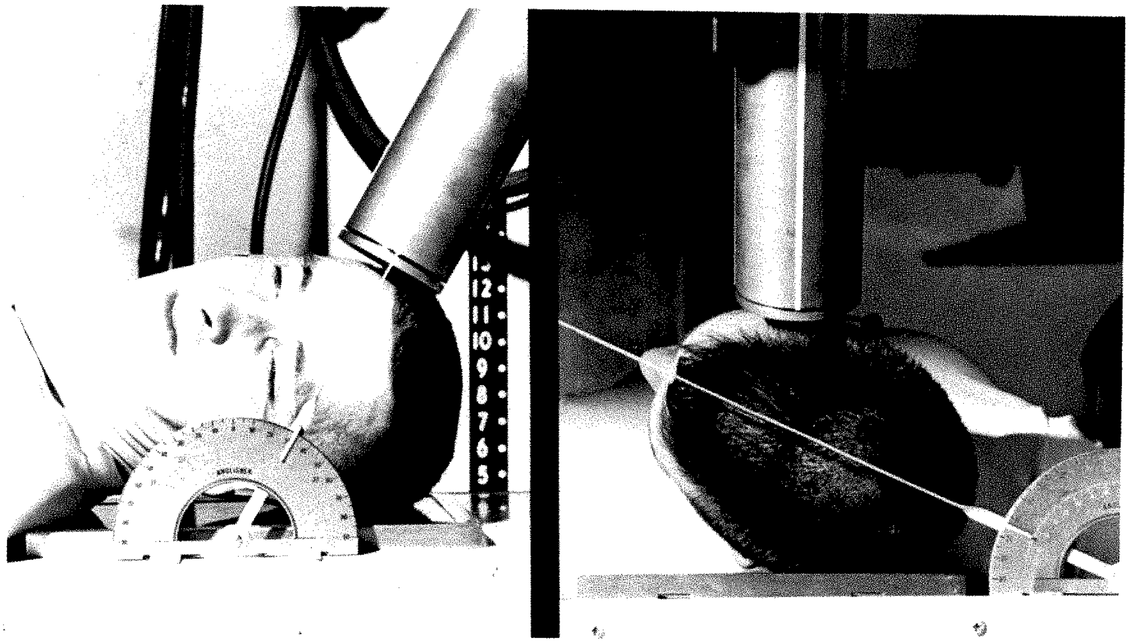


Fig. 19. Patient positioned for Owen's modification of Mayer's axial projection.

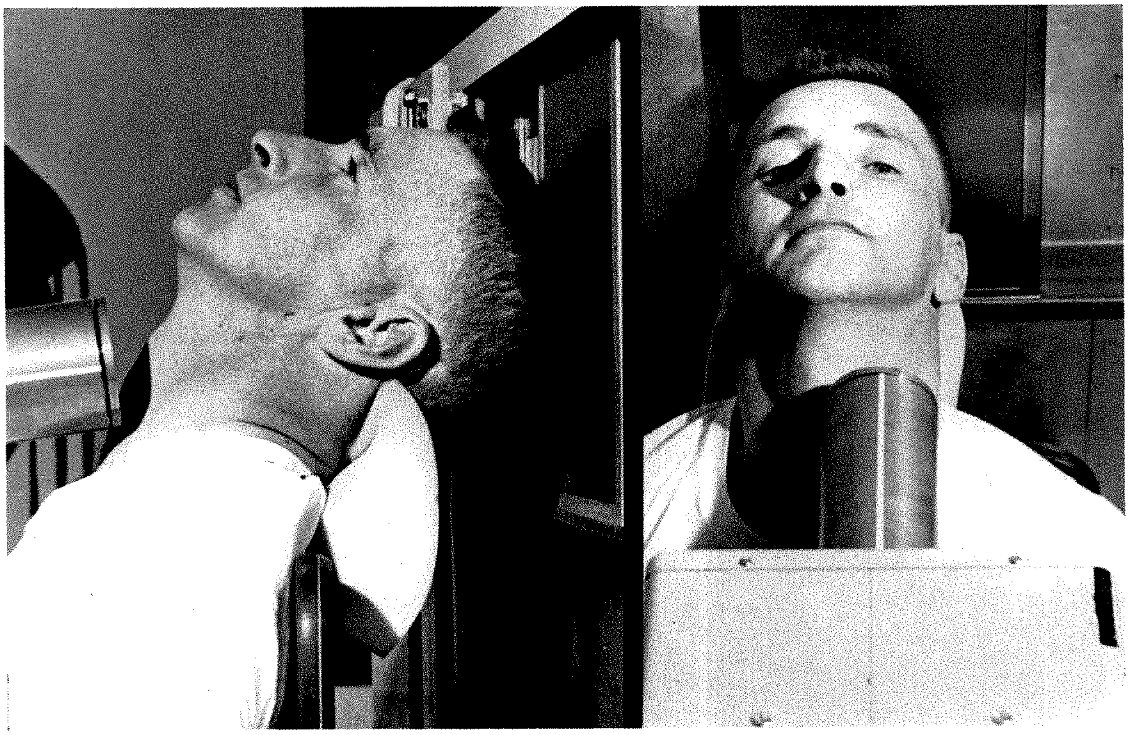


FIG. 21. Patient positioned for the unilateral submento-vertical (basal) projection.

at 90 degrees the tympanic cavity may be obscured by the condyle of the mandible, while Figure 24 demonstrates complete visualization at 105 degrees. This is the typical appearance of the structures as seen in the basal view.

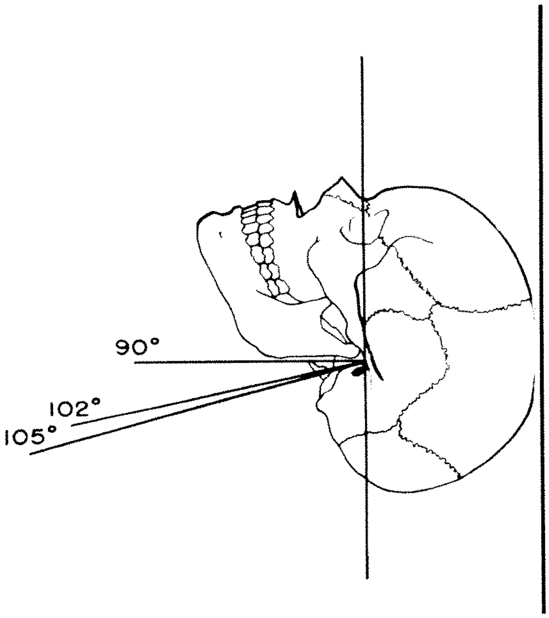


FIG. 22. Diagram showing the angle variations in the submento-vertical (basal) projection necessary to demonstrate tympanic cavity and ossicles.

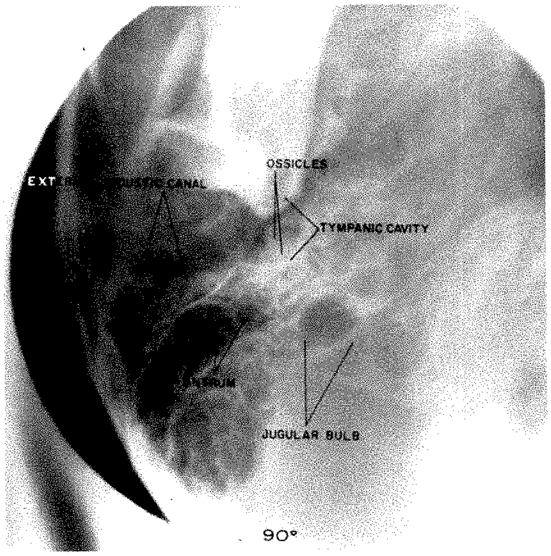


FIG. 23. Submento-vertical roentgenogram at 90° shows that the tympanic cavity may be obscured.

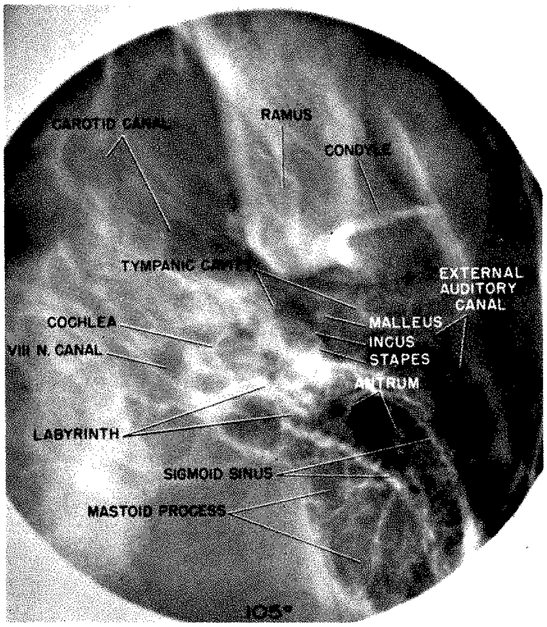


Fig. 24. Submento-vertical roentgenogram at 105° shows complete visualization of the tympanic cavity.

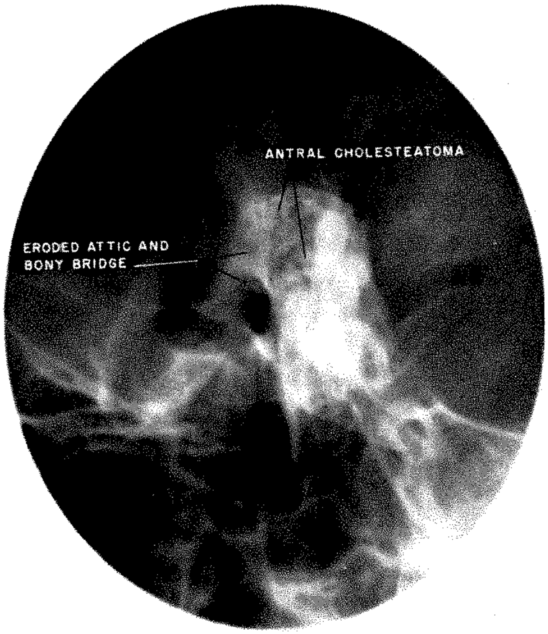


Fig. 26. Same case as in Figure 25 using Owen's projection, showing similar changes.

ILLUSTRATIVE CASES

Figure 25 is a roentgenogram using the Mayer projection in a 28 year old man with foul discharge from his right ear and dizziness for the previous 10 or 12 years. It shows preservation of the bony bridge but erosion in the attic and mastoid antrum with a number of thick walled cells remaining. Similar changes are demonstrated in the Owen projection (Fig. 26). The best delineation of the pathologic process in this patient, however, was obtained in the Chamber-

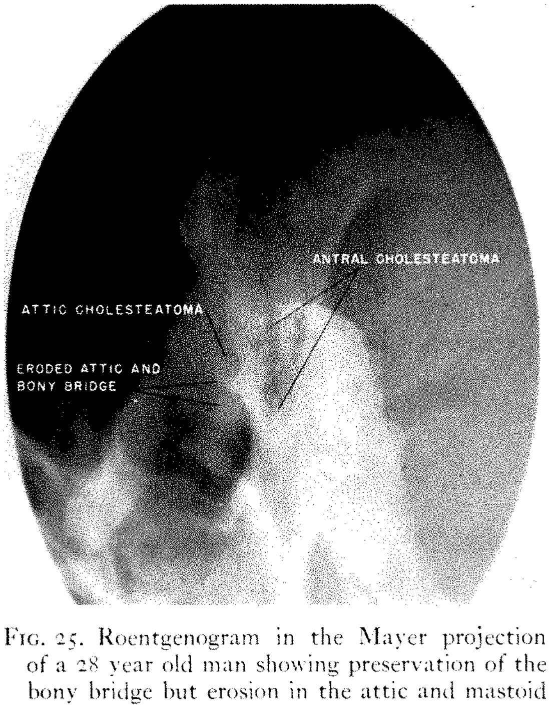


Fig. 25. Roentgenogram in the Mayer projection of a 28 year old man showing preservation of the bony bridge but erosion in the attic and mastoid antrum with a number of thick walled cells remaining.

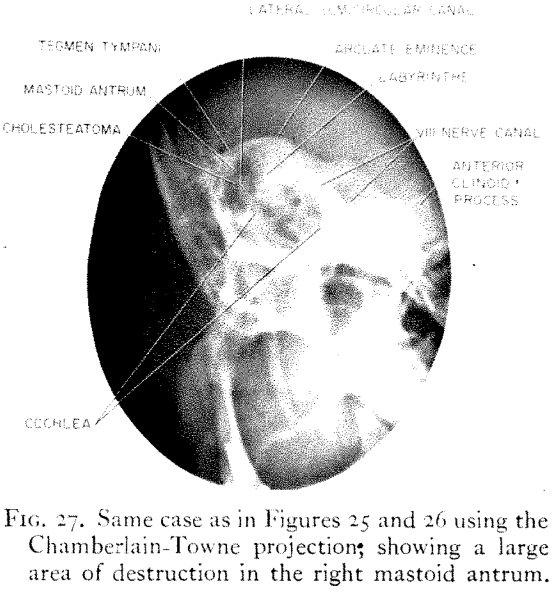


Fig. 27. Same case as in Figures 25 and 26 using the Chamberlain-Towne projection; showing a large area of destruction in the right mastoid antrum.

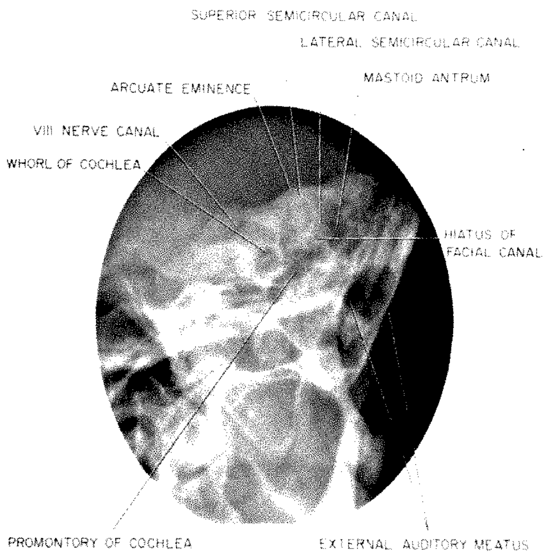


Fig. 28. Same as in Figures 25, 26, and 27 showing slight sclerosis of the periantral cells in the left ear.

lain-Towne projection (Fig. 27), where a large area of destruction from cholesteatoma in the right mastoid antrum was seen adjacent to the horizontal semicircular canal. Figure 28 shows slight sclerosis of the periantral cells in the left ear. The normal roentgen anatomy of the structures is beautifully demonstrated.

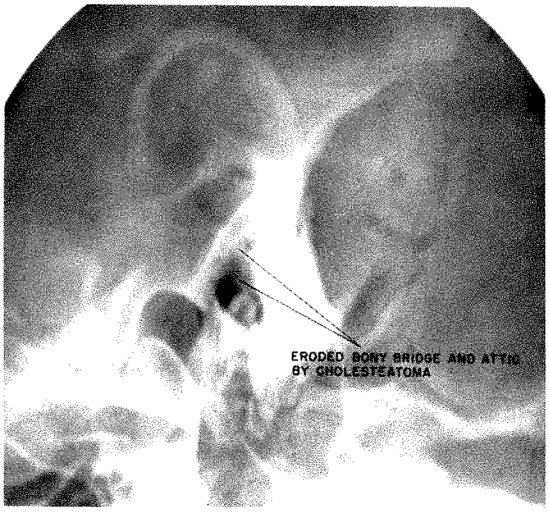


Fig. 29. Roentgenogram in the Owen projection of a 27 year old woman showing loss of bony bridge and irregular erosion of the epitympanic space or attic with widening of the aditus and extension into the mastoid of the right ear.

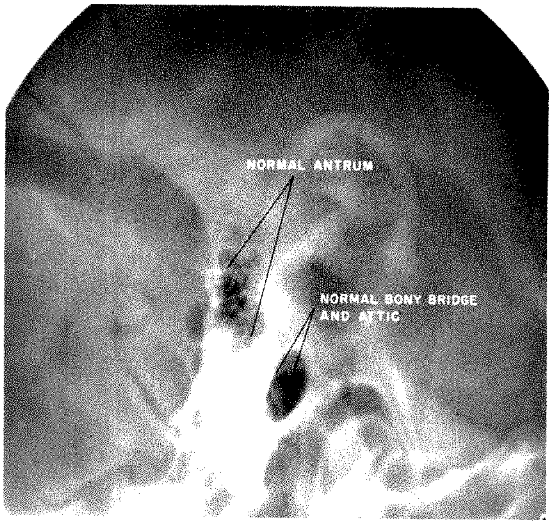


Fig. 30. Same case as in Figure 29 shows preservation of the bony bridge and a normal epitympanic space, aditus and mastoid antrum of the left ear.

Another patient, a woman of 27 years of age, had a history of a throbbing pain in her right ear and head for 20 years with chronic ear discharge. On Owen's projection (Fig. 29) loss of the bony bridge and irregular erosion of the epitympanic space or attic with widening of the aditus and extension into the mastoid antrum, where there was considerable periantral sclerosis, were demonstrated. A roentgenogram of the

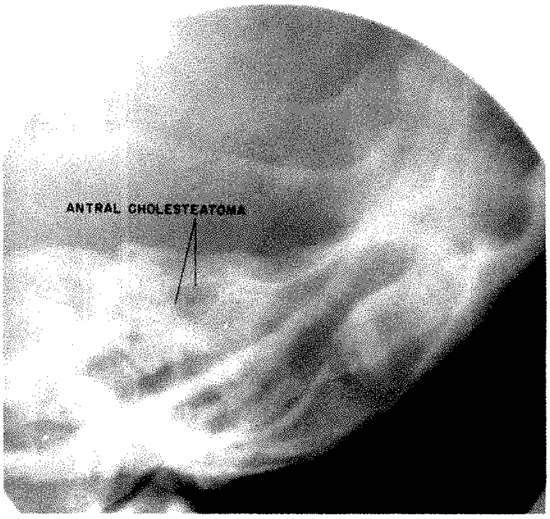


Fig. 31. Same case as in Figures 29 and 30 using Stenvers' projection. There is minimal evidence of an antral cholesteatoma.

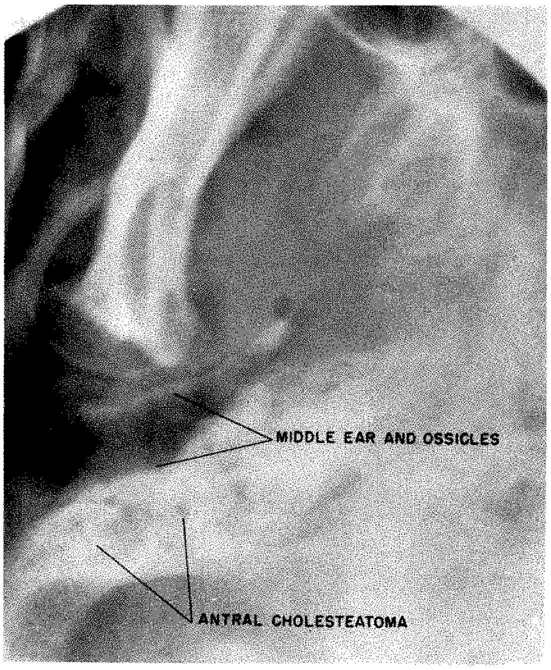


Fig. 32. Same case as in Figures 29, 30, and 31 using the submento-vertical basal projection. There is minimal evidence of an antral cholesteatoma.

left ear made for comparison (Fig. 30) showed preservation of the bony bridge and a normal epitympanic space, aditus and mastoid antrum.

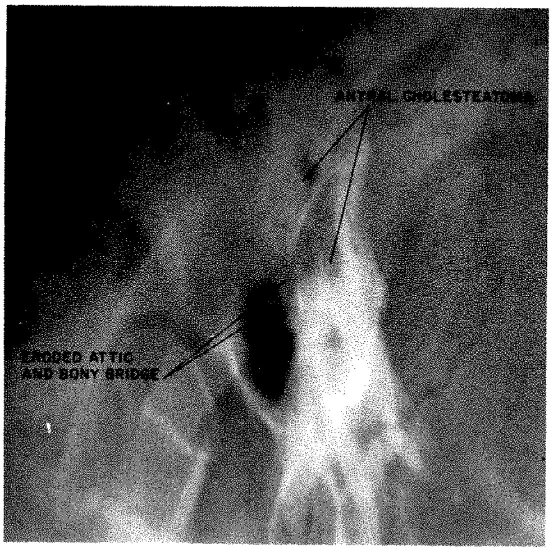


Fig. 33. Roentgenogram in Mayer's projection of a 27 year old woman showing erosion extending through the attic and a widened aditus into the antrum with osseous destruction.

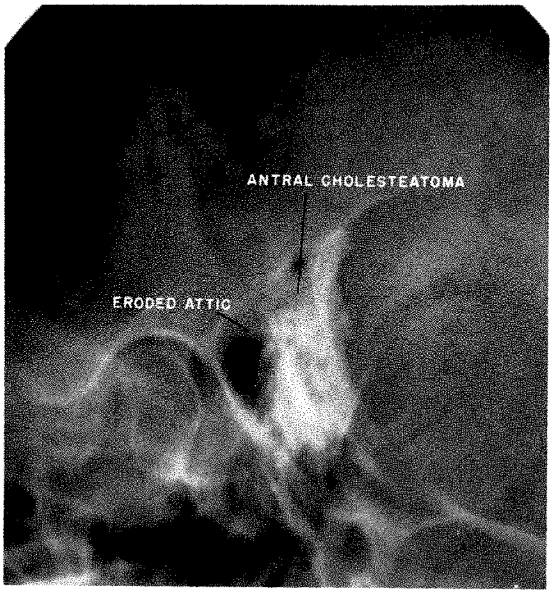


Fig. 34. Same case as in Figure 33 using Owen's projection. The same roentgen findings are noted.

Minimal evidence of an antral cholesteatoma was seen in the Stenvers' (Fig. 31) and basal views (Fig. 32).

In the next patient, a woman of 27 years of age with a malodorous discharge from her right ear for 14 years, the Mayer view at 35 degrees demonstrated the tympanic cavity very well and showed erosion extending through the attic, and a widened aditus into the antrum with osse-

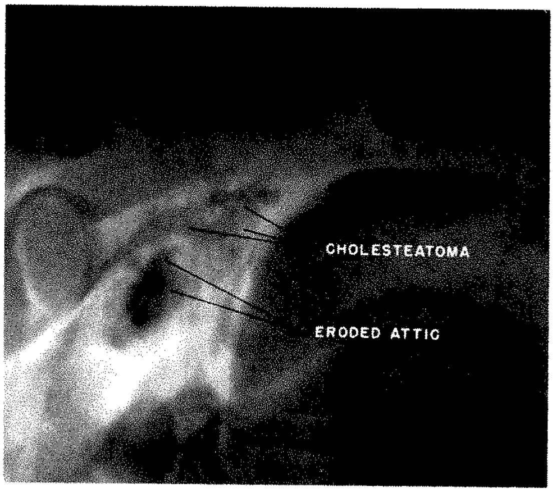


Fig. 35. Same case as in Figures 33 and 34 using the Schüller projection. Erosion of the epitympanic space extends into the region of the antrum.

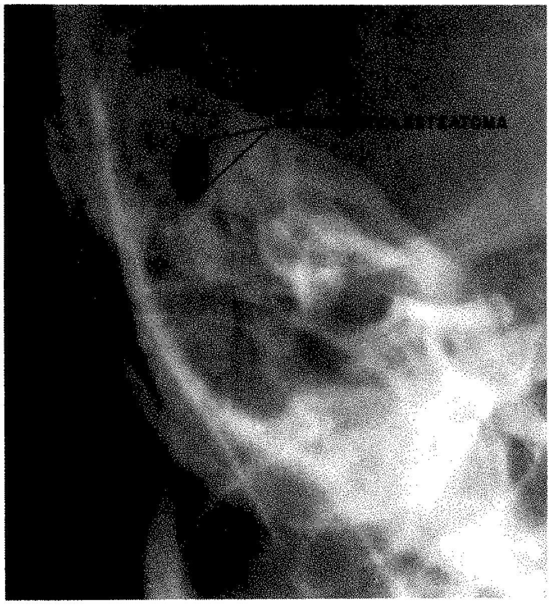


Fig. 36. Same case as in Figures 33, 34, and 35 using the Chamberlain-Towne projection. There is strong evidence of cholesteatoma.

ous destruction indicative of cholesteatoma (Fig. 33). This was also shown in a 25 degree Owen's projection (Fig. 34) and a 30 degree Schüller's projection (Fig. 35), where erosion of the attic or epitympanic space was seen extending into the region of the mastoid antrum. Operation confirmed the presence of granulation tissue and cholesteatoma. The findings in the Chamberlain-Towne projection at 35 degrees indicated strong evidence of cholesteatoma (Fig. 36).

Finally, a young man of 30 years of age with chronic purulent drainage from both ears was examined, and the importance of varying the angle of projection was clearly shown in this case. At an angle of 45 degrees ventro-dorsal (Fig. 37), the tympanic cavity and the epitympanic space were completely obscured by the mastoid process. A reduction of 10 degrees to 35 degrees still showed the edge of the mastoid process overlapping at least one-half of the tympanic cavity. At 30 degrees the middle ear was visualized but not fully, at 25 degrees more so, at 20 degrees it was somewhat better, but only at 15 degrees was it completely demonstrated. Then the full extent of the pathologic changes, erosion of the epitympanic space and extension of the disease process into the mastoid antrum, was observed.

SUMMARY

The basic roentgen anatomy is roentgenographically illustrated and the need for precision roentgenography in delineating pathologic alterations of the middle ear and mastoid processes is stressed.

Lewis E. Etter, M.D.
Western Psychiatric Institute
and The Falk Clinic
University of Pittsburgh School of Medicine
Pittsburgh 13, Pennsylvania

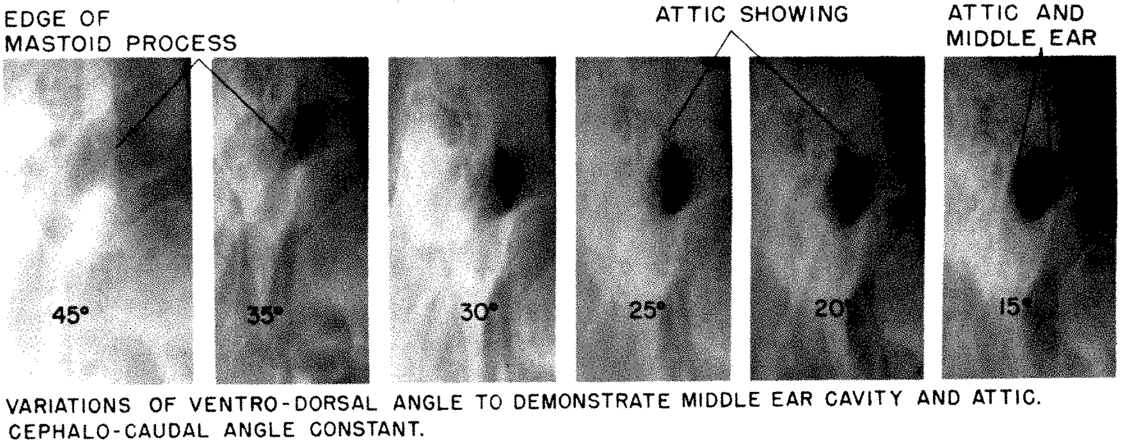

EDGE OF MASTOID PROCESS
ATTIC SHOWING
ATTIC AND MIDDLE EAR
45°
35°
30°
25°
20°
15°
VARIATIONS OF VENTRO-DORSAL ANGLE TO DEMONSTRATE MIDDLE EAR CAVITY AND ATTIC.
CEPHALO-CAUDAL ANGLE CONSTANT.

Fig. 37. Studies of a 30 year old man showing the importance of varying the ventro-dorsal angle for the most satisfactory demonstration of the middle ear cavity and attic. The cephalo-caudal angle remains constant. •

REFERENCES

1. BAST, T. H., and ANSON, B. J. The Temporal Bone and the Ear. Charles C Thomas, Publisher, Springfield, Ill., 1949.
2. CHAUSSÉ, C. Trois incidences pour l'examen du rocher. *Acta radiol.*, 1950, *34*, 274–287.
3. COMPERE, W. E., JR. Interesting aspects of radiography of temporal bone. *Tr. Pacific Coast Oto-Ophth. Soc.*, 1957, *38*, 253–258.
4. COMPERE, W. E., JR. Tympanic cavity clearance studies. *Tr. Am. Acad. Ophth.*, 1958, *62*, 444–454.
5. COMPERE, W., and OWEN, G. Radiologic examination of mastoid, middle ear and eustachian tube. Instruction bulletin. *Am. Acad. Ophth.*, 1958.
6. COMPERE, W. E., JR. Roentgenologic aspects of tympanoplasty; otologist's viewpoint. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1959, *81*, 956–963.
7. FLETCHER, H. G., and WINDHOLZ, F. Use of x-ray in chronic mastoid conditions. *Laryngoscope*, 1946, *56*, 602–611.
8. MACMILLAN, A. S. Cholesteatoma in chronic otitis media. AM. J. ROENTGENOL. & RAD. THERAPY, 1936, *36*, 747–750.
9. MAYER, E. G. Technic of roentgenologic examination of temporal bone. *Radiology*, 1926, *7*, 306–317.
10. MAYER, O. Die Mastoiditis nach Untersuchungen von ganzen Felsenbeinen und Knochensplittern. *Ztschr. Hals- Nasen- u. Ohrenh.*, 1927–1928, *18*, 628–651.
11. OWEN, G. R. Simplified method of producing axial view of Mayer in chronic mastoiditis and attic cholesteatoma. AM. J. ROENTGENOL. & RAD. THERAPY, 1947, *57*, 260–263.
12. OWEN, G. R. Key area (attic-aditus-antrum) in chronic mastoid. *Tr. Am. Otol. Soc.*, 1951, *39*, 189.
13. PENDERGRASS, E. P., SCHAEFFER, J. P., and HODES, P. J. The Head and Neck in Roentgen Diagnosis. Second edition. Charles C Thomas, Publisher, Springfield, Ill., 1956.
14. PENDERGRASS, E. P., HODES, P. J., TONDREAU, R. L., and MARDEN, P. A. Tympanic cavity and auditory ossicles; roentgen findings in health and disease. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1956, *76*, 327–342.
15. RUNSTRÖM, G. Roentgenological study of acute and chronic otitis media. *Acta radiol.*, 1933, Suppl. 17, 1–88.
16. SHAMBAUGH, G. E., JR. Surgery of the Ear. W. B. Saunders Company, Philadelphia, 1959.
17. STENVERS, H. W. Roentgenology of os petrosum. *Arch. Rad. & Elec.*, 1917, *22*, 97–119.
18. TOWNE, E. B. Erosion of petrous bone by acoustic nerve tumor; demonstration by roentgen ray. *Arch. Otolaryng.*, 1926, *4*, 515–519.
19. WALTNER, J. G. Roentgen diagnosis of cholesteatoma of middle ear. AM. J. ROENTGENOL. & RAD. THERAPY, 1949, *62*, 674–684.
20. YOUNG, B. R. The Skull, Sinuses and Mastoids; A Handbook of Roentgen Diagnosis. Year Book Publishers, Inc., Chicago, 1948.

* * *

TECHNIQUE FOR THE STUDY OF THE MIDDLE EAR*

WITH SPECIAL REFERENCE TO CHOLESTEATOMA

By ANDRÉ SANSREGRET, M.D.†
MONTRÉAL, QUÉBEC, CANADA

THE purpose of this paper is to describe a roentgenographic technique, using a tube with a fine focal spot (0.3 mm.) and employing one of three projections or a combination of them for the accurate diagnosis of a number of middle ear lesions, when laminagraphy is not available.

TECHNIQUE

The three projections are: (1) the Chaussé III projection,[4] (2) the Guillen or unilateral transorbital projection,[8,16] and (3) the Schüller II or bilateral transorbital projection. For all three projections the patient is placed in a supine position. A radiolucent cushion is used to raise the head and the chin is drawn in.

(1) CHAUSSÉ III PROJECTION

The central ray is directed slightly above and lateral to the superolateral margin of the orbit. It passes through the tragus and falls perpendicular to the roentgenographic plane. This brings the horizontal plane of the head to an angle of nearly 30° with the central ray. (The horizontal plane represents a line drawn between the inferior orbital margin and the tragus—Virchow's plane.) The head is turned toward the opposite side, the sagittal plane of the skull forming an angle of about 8° with the central ray. Because of individual variations, 3 roentgenograms are obtained: one with the sagittal plane at 8° to the central ray, another at 10° and the third one at 12°. In certain instances, additional angulation may be required (Fig. 1, *A–D*).

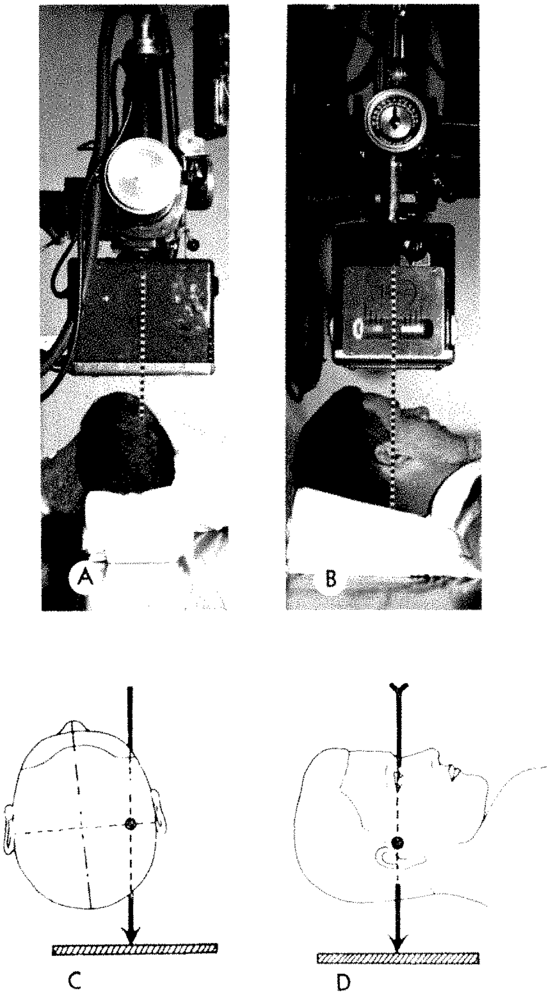


FIG. 1. (*A–D*) Chaussé III projection. The head is raised and the chin is drawn in so that the central ray enters above and lateral to the superolateral margin of the orbit, passes through the tragus and falls perpendicular to the roentgenographic plane. The sagittal plane of the skull is angulated towards the opposite side 8°, 10°, and 12° to the central ray, and a roentgenogram is taken at each angle.

The Chaussé III projection gives an ex-

---

* Presented in abridged form at the Tenth International Congress of Radiology, August 26–September 1, 1962, Montréal, Québec, Canada.

† Radiologist, Hôpital Maisonneuve, Montréal, Québec, Canada.

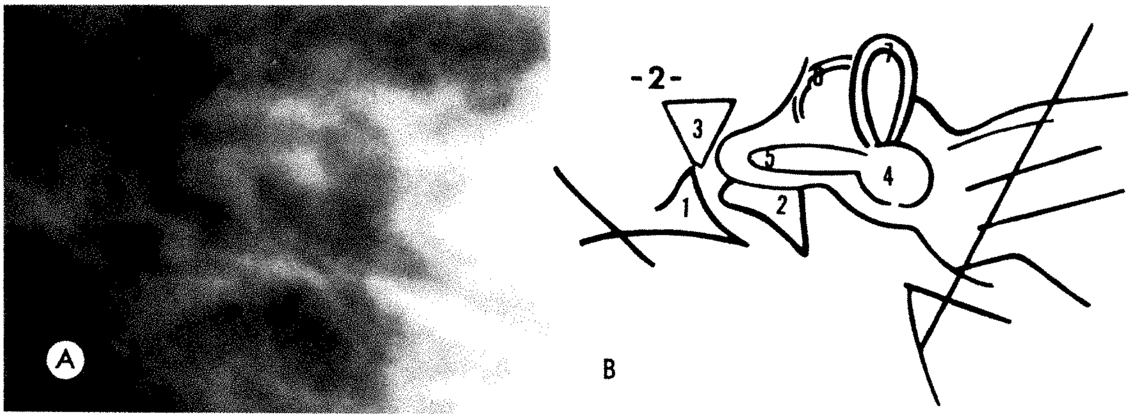


Fig. 2. (*A*) Chaussé III projection. (*B*) Diagram of *A*. (1) Attic wall; (2) ossicles: malleus and incus; (3) epitympanic recess (antral area); (4) vestibule; (5) lateral semicircular canal; (6) posterior semicircular canal; and (7) superior semicircular canal.

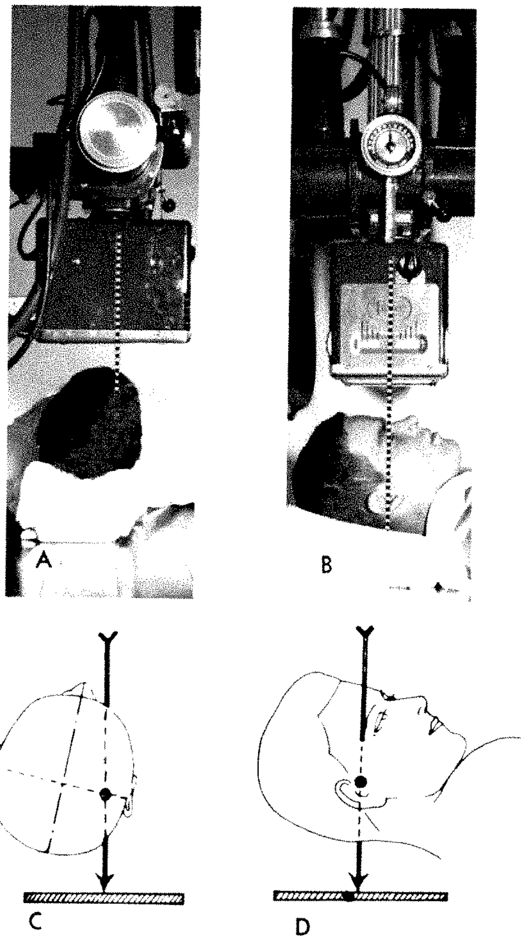
cellent tangential view of the edge of the attic wall (Fig. 2, *A* and *B*).

(2) GUILLEN OR UNILATERAL TRANSORBITAL PROJECTION

The central ray is directed to the superomedial aspect of the orbit, 8 mm. above the inner canthus of the eye. It traverses through the tragus and falls perpendicular to the roentgenographic plane. The head is turned toward the side under examination, the sagittal plane of the skull forming an angle of 12° to 15° with the central ray. Here again, more than 1, usually 2, roentgenograms are taken at slightly different angles (Fig. 3, *A–D*).

The Guillen projection gives an excellent tangential view of the medial part of the labyrinth (Fig. 4, *A* and *B*).

In both the Chaussé III and Guillen projections the intracranial landmark is the same. It is referred to as the "attic point" (related to the head of the malleus). This point is located 2.5 cm. medial to either end of the bi-auricular line.



»»→

Fig. 3. (*A–D*) Guillen or unilateral transorbital projection. The head is raised so that the central ray enters at the superomedial aspect of the orbit 8 mm. above the inner canthus of the eye, passes through the tragus and falls perpendicular to the roentgenographic plane. The sagittal plane of the skull is angulated towards the side examined 12° to 15° to the central ray, and a roentgenogram is taken at each angle.

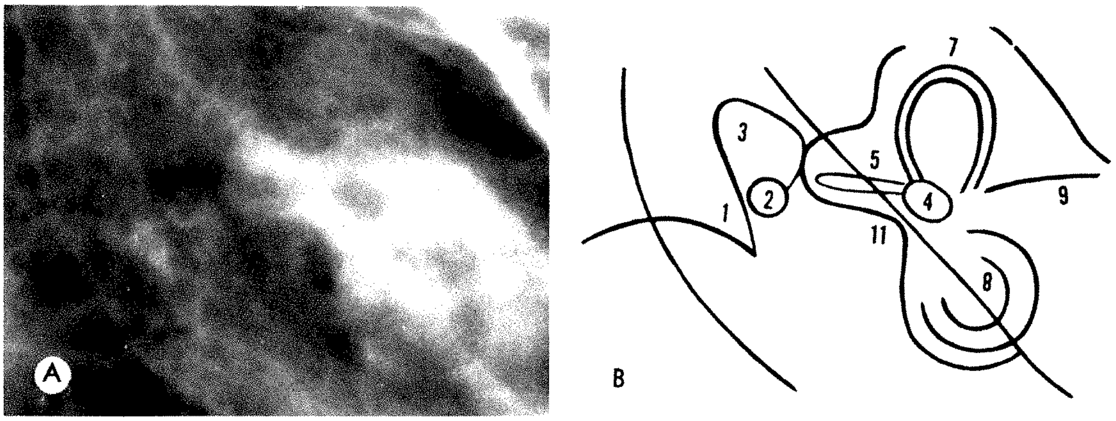


Fig. 4. (*A*) Guillen projection. (*B*) Diagram of *A*. (1) Attic wall; (2) superimposed ossicles: malleus and incus; (3) epitympanic recess; (8) cochlea; (9) internal meatus; and (11) fenestra vestibuli.

(3) SCHÜLLER II OR BILATERAL TRANSORBITAL PROJECTION

In this projection, the sagittal plane of the skull is not augulated; it is a true anteroposterior view with the head lifted and the chin drawn in as in the Chaussé III projection. The central ray is directed to the bridge of the nose and falls perpendicular to the roentgenographic plane (Fig. 5, *A–D*).

ADDITIONAL PROJECTIONS

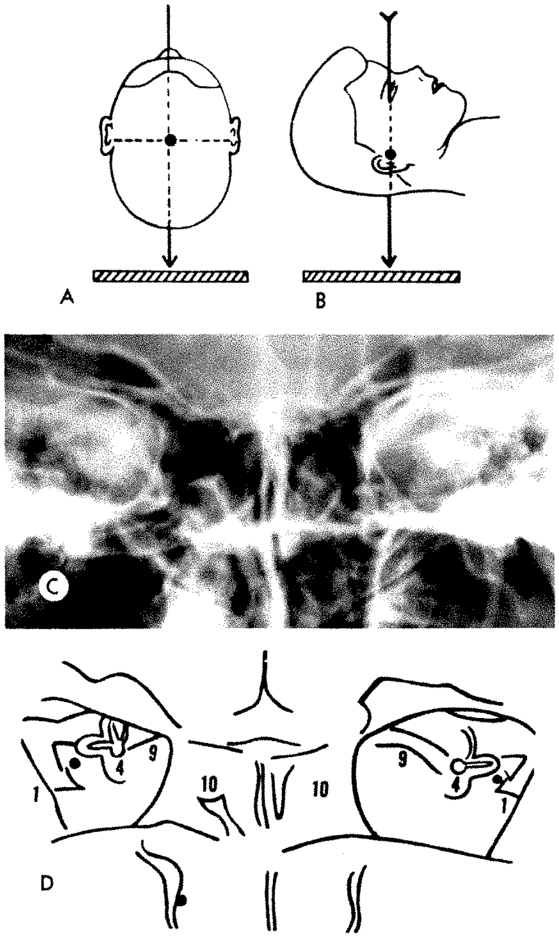
A routine Towne projection and the two routine Schüller projections are also used to complete the examination and to provide some useful detail of the mastoid cells.

MATERIAL

Sixty-six cases of cholesteatomas as well as 17 lytic inflammatory processes of the middle ear, all surgically proved, were studied by means of roentgenograms in the Chaussé III and the Guillen projections. We have found our technique useful in cases of otosclerosis and congenital malformations as well.

(A) CHOLESTEATOMA OF THE ATTIC WALL

Twelve cases of cholesteatoma were confined or limited to the attic wall. In 66.3 per cent (8 out of 12 cases), the roentgeno-



←

Fig. 5. Schüller II or bilateral transorbital projection. (*A* and *B*) Diagram showing the projection used. (*C*) Anteroposterior view, 30° angulation. (*D*) Diagram of *C*. Essentially the same structures are projected into each orbit.

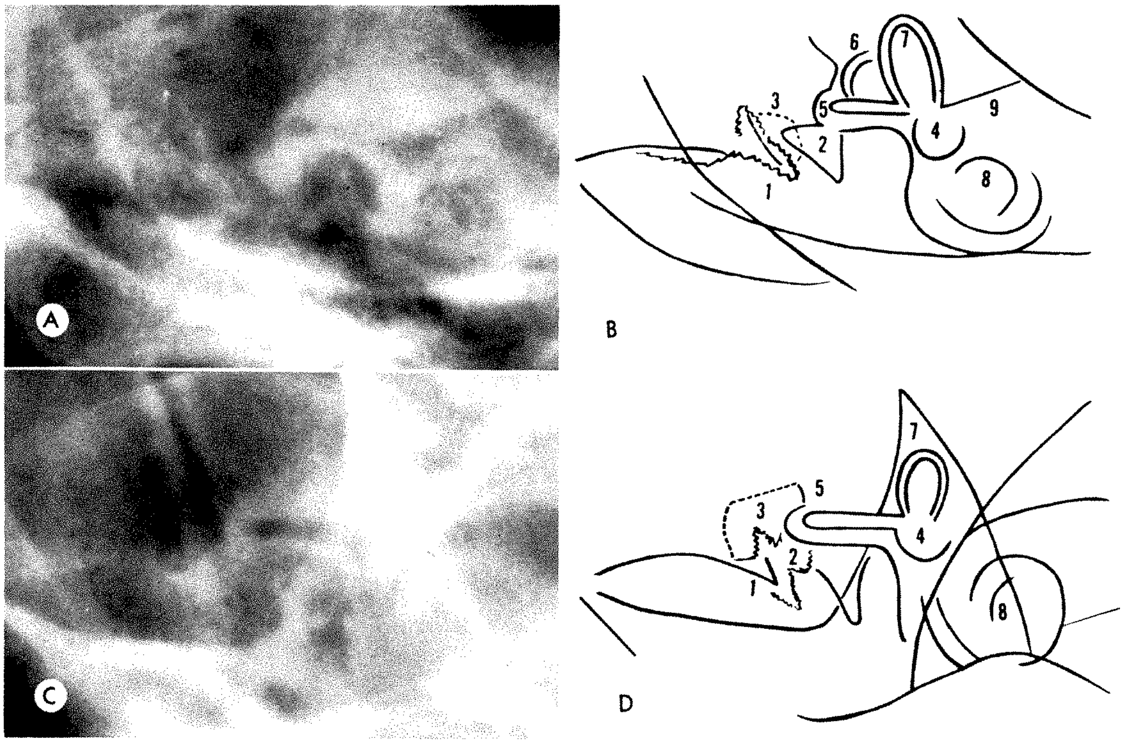


Fig. 6. Case I. Cholesteatoma of the attic wall. (*A*) Chaussé III projection. (*B*) Diagram of *A*. (1) Haziness and blurring of the attic wall; (2) blurred interspace between the ossicles and attic wall; (3) poorly visualized epitympanic recess. (*C*) Guillen projection. (*D*) Diagram of *C*. (1) Haziness of the attic wall; (2) poorly delineated ossicles; (3) poorly demonstrated epitympanic recess.

logic diagnosis was established prior to surgery.

Case I. C.J.P., a 17 year old patient, was admitted because of purulent nocturnal discharge from the left ear. There was no pain and the hearing was not impaired.

On examination, it was found that the ear drum was obscured by purulent adhesive matter, which could not be cleansed completely.

Roentgenograms (Fig. 6, *A–D*) showed a haziness and blurring of the attic wall, as well as of the interspace between the ossicles and the attic wall. The ossicles were not clearly outlined. The epitympanic recess was poorly visualized. A diagnosis of an inflammatory process, probably lytic, and particularly marked at the attic wall was made.

An atticotomy was performed. The edge of the lateral wall of the attic was resected and a pocket of pearly white epithelial debris, characteristic of cholesteatoma was removed. The ossicles were not involved by the lytic process. The antrum was exposed and found to be very small and fairly normal. The diagnosis at surgery was cholesteatoma of the attic wall.

Comment. A study of our cases revealed certain distinguishing roentgenographic features of cholesteatoma of the attic wall, which we believe to be equally valuable in the examination of the middle ear by means of laminagraphy.[20] These consist of erosion localized in the attic or the supratympanic portion of the attic. The attic wall is irregular, blurred and sclerosed. The interspace between the attic and the ossicles in some instances is likewise blurred.

(B) CHOLESTEATOMA OF THE ADITUS (ATTIC WALL AND OSSICLES)

Twenty-three cases of adital cholesteatoma were studied, of which 20 (86.9 per cent) were diagnosed roentgenologically prior to surgery.

Case II. L.C., a 37 year old patient, had been operated on for an antral cholesteatoma of the left ear 1 year previously. He was readmitted to the hospital because of a purulent discharge from the right ear, which had been present since the age of 14. Examination revealed a large centro-marginal perforation through which it was possible to probe as far as the attic. The audiogram disclosed a partial loss of hearing.

Roentgenograms (Fig. 7, *A* and *B*) showed a haziness of the attic wall and a lytic process of the area. The ossicles were also involved by a lytic process. There was blurring of the interspace between the ossicles and the attic wall and a clear space between the ossicles and the bony labyrinth. The epitympanic recess was not well demonstrated. A roentgenologic diagnosis was made of an inflammatory and probably lytic process involving the attic wall and, more especially, the ossicles.

Radical mastoidectomy and tympanoplasty were performed. The exposed antrum was found to be fairly normal. On the lateral wall of the attic, an osteolytic process about 2 mm. in width was present. The handle of the malleus and part of the incus were destroyed by an osteolytic process. The stapes was completely destroyed. The pathologist reported cholesteatoma involving the lateral wall of the attic and the ossicles.

Case III. S.D., a 44 year old patient, was admitted because of a purulent discharge from the right ear. Audiometry revealed gross loss of hearing. The ear drum was red and retracted but no pin point perforation was seen.

Roentgenograms (Fig. 8, *A–D*) showed a lytic process and a haziness of the attic wall. The ossicles were almost completely destroyed. The adital area was enlarged but the epitympanic recess was still visible. A roentgenologic diagnosis of a lytic inflammatory process of the adital area was made.

A radical mastoidectomy was performed. The widely exposed antral region revealed no cholesteatoma; however, inflammatory scarred tissue was found involving the entire middle ear. The diagnosis at surgery was lytic inflammatory process of the adital area involving the whole middle ear, without evidence of cholesteatoma.

Comment. It must be pointed out that roentgenographically it is impossible to distinguish between a cholesteatoma and a lytic inflammatory process of the attic wall or of the adital area; however, for practical purposes this is irrelevant since the distinction does not influence the surgical procedure.

Roentgenographically, in cholesteatoma of the adital area the ossicles appear to be hazy, eroded or even destroyed. A clear space may be demonstrated between the ossicles and the lateral semicircular canal.[15] Widening of the aditus appears to be one of the important features. The epitympanic recess may not be visualized and the fenestra vestibuli is blurred.

(c) CHOLESTEATOMA OF THE ANTRAL AREA

Out of 31 cases of cholesteatoma of the antral area which were operated on, 26 (83.9 per cent) were diagnosed prior to operation. It is our opinion that with ex-

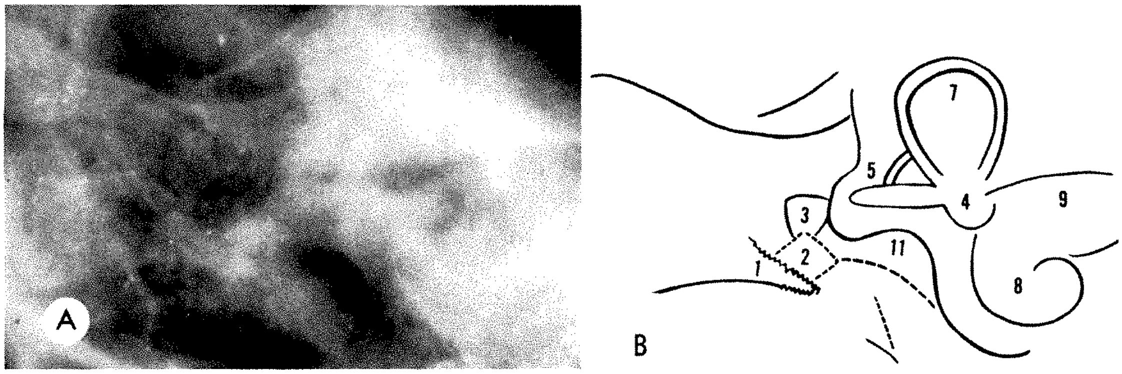


Fig. 7. Case II. Cholesteatoma of the adital area. (*A*) Guillen projection. (*B*) Diagram of *A*. (1) Haziness of the attic wall and lytic process of the same area; (2) lytic process of the ossicles, blurred interspace between the ossicles and the attic wall and a clear space between the ossicles and bony labyrinth; (3) faint visualization of the epitympanic recess.

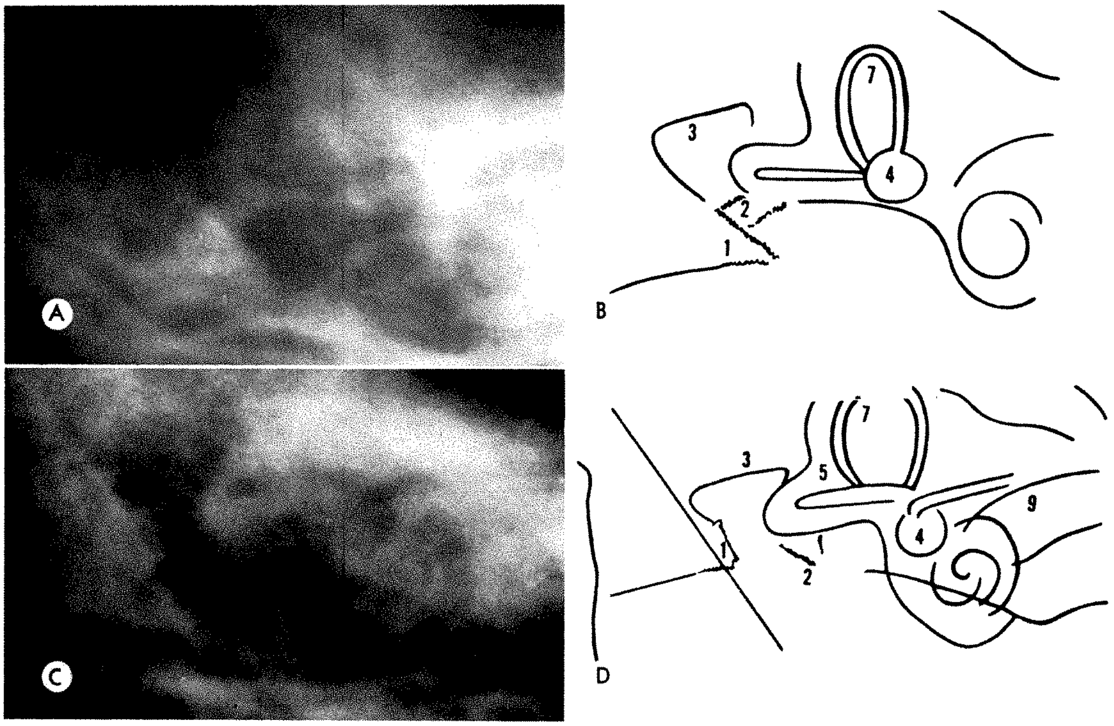


Fig. 8. Case iii. Lytic inflammatory process of the adital area. (*A*) Chaussé iii projection. (*B*) Diagram of *A*. (1) Haziness of the attic wall; (2) almost completely sloughed ossicles; (3) good visualization of the epitympanic recess. (*C*) Guillen projection. (*D*) Diagram of *C*. (1) Lytic process of the attic wall; (2) complete destruction of the ossicles and enlarged adital area; (3) epitympanic recess still visible.

perience more than 90 per cent of these cases should be diagnosed prior to surgery.

Case iv. P.F., a 37 year old male, was admitted to the hospital because of a purulent discharge from the right ear which had been present for the past 30 years. The ear drum was totally destroyed by a cholesteatoma. Two large polyps were seen posteriorly.

On roentgenograms (Fig. 9, *A–D*) the attic wall was found to be sclerotic and eroded. The ossicles were also eroded and an increased density was noted. The interspace between the ossicles and the attic wall was not visualized. A clearly delineated oval area, above the epitympanic recess, was present which was believed to represent a cholesteatoma in the antral area.

A radical mastoidectomy was performed. The antral region and the attic wall were found to be replaced by a large cholesteatoma. There was almost complete sloughing of the malleus and the incus, and what remained of them was removed. The stapes was left in place. A diagnosis of cholesteatoma of the antral region involving the attic wall and the ossicles was made.

Case v. L.A., a 49 year old male, was admitted to the hospital because of a purulent discharge from the left ear for the past 5 years. Audiometry revealed gross loss of hearing. During the previous 3 weeks, the patient experienced vertigo, tinnitus and vomiting.

The ear drum was completely destroyed and debris were found. The attic wall was easily probed. The lateral semicircular canal was invaded by a cholesteatoma and presented a visible fistula.[16,24]

Roentgenograms (Fig. 10, *A–D*) showed an irregular and sclerotic attic wall. The ossicles were completely destroyed. The antral area was enlarged and oval in shape. A fistula of the lateral semicircular canal was noted. The roentgenologic diagnosis was cholesteatoma of the antral region.

A right radical mastoidectomy revealed a large cholesteatoma of the antral region, involving also the entire middle ear. The malleus was almost completely destroyed. The fistula of the lateral semicircular canal was well seen. The diagnosis was cholesteatoma of the antral

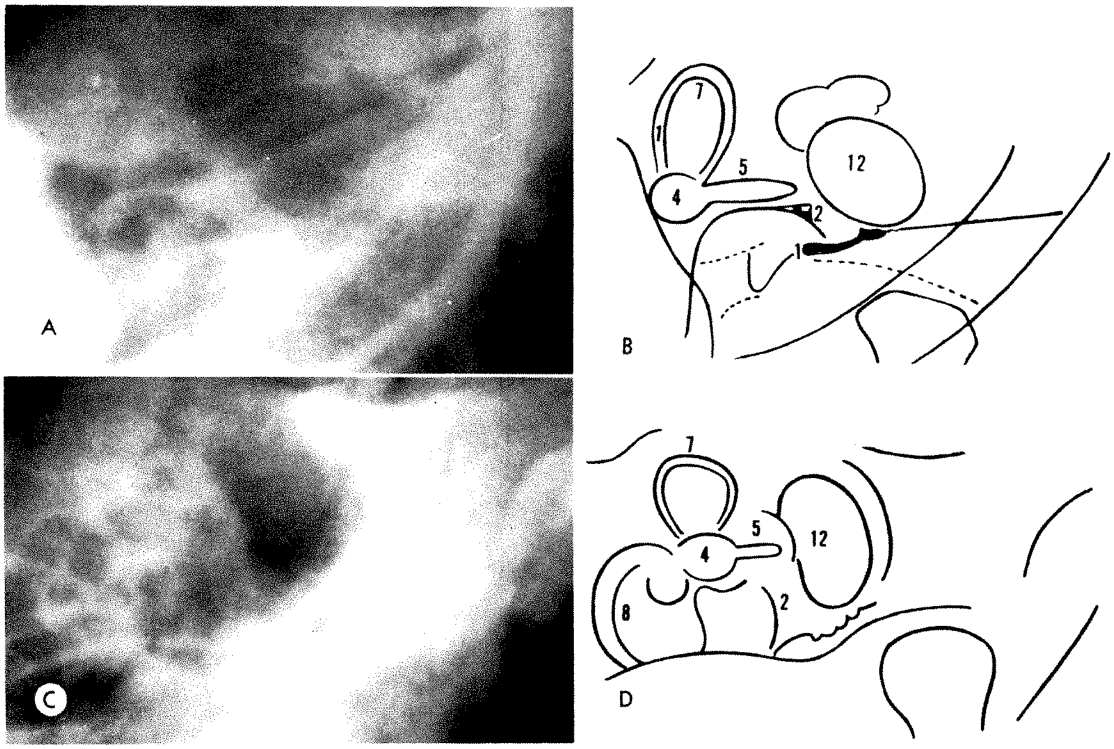
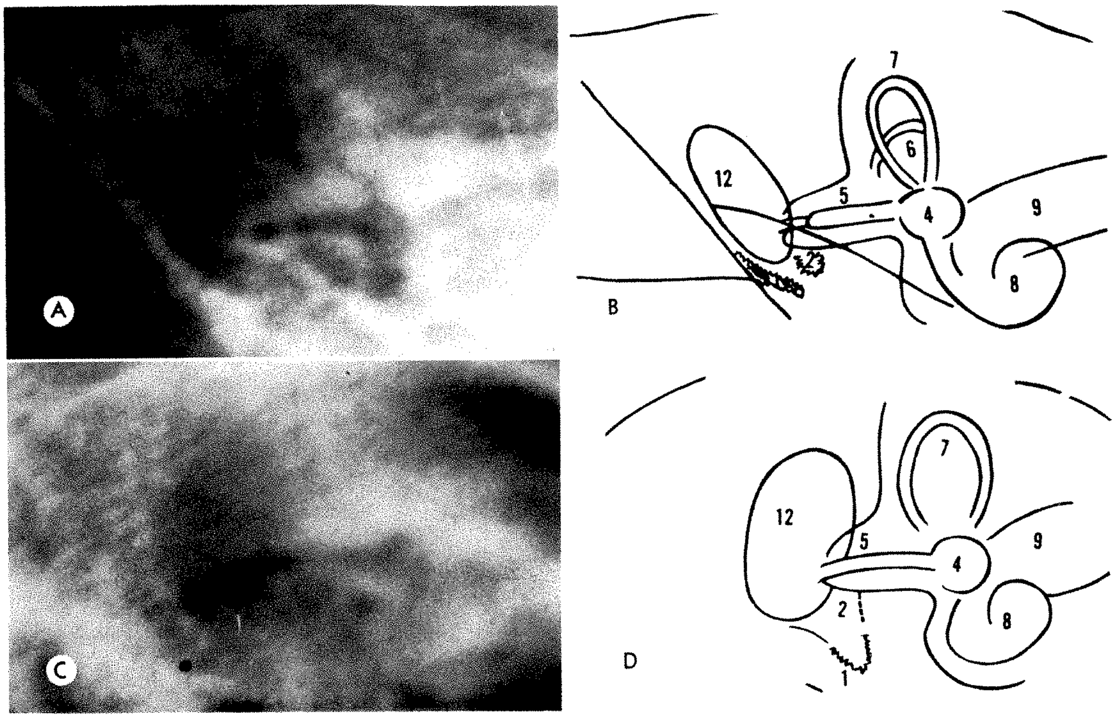


FIG. 9. Case IV. Cholesteatoma of the antral area. (*A*) Chaussé III projection. (*B*) Diagram of *A*. (1) Sclerosis and erosion of the wall of the attic; (2) erosion of the ossicles and increased density. The interspace between the ossicles and the attic wall is no longer visualized; and (12) a clear-cut oval area over the epitympanic recess is seen. (*C*) Guillen projection. (*D*) Diagram of *C*. Same findings as in *B*.



region involving the middle ear and a fistula of the lateral semicircular canal.

Comment. A roentgenographic feature associated with cholesteatoma of the antral region is a clear oval defect, sometimes as small as 6×4 mm. It is well circumscribed and sharply outlined. There may be erosion of the lateral or posterior semicircular canal. We believe that a positive diagnosis of cholesteatoma of the antral region should be made prior to surgery since the operative approach to a cholesteatoma in this region may well differ from that of a cholesteatoma in the adital region.

A well delineated oval clear area of the antral region should be differentiated from a large, still more or less conical epitympanic recess. Where there is a large epitympanic recess, the attic wall and the ossicles will be normal and well preserved.[1] One such proven case is shown in Figure 11, *A* and *B*.

In a former study, Jensen[10] diagnosed 71.4 per cent of his cases of cholesteatoma of the antral region prior to surgery by using the Chaussé III projection alone. We now believe that these results can be improved with the routine use of the combined Chaussé III and Guillen projections.

Small fistulas of the lateral semicircular canal are also quite easily seen in these projections, especially on the Chaussé III view.

(D) CONDITIONS OTHER THAN CHOLESTEATOMA

Otosclerosis. The use of the described technique has also proved beneficial in studying cases of otosclerosis. In these cases, the mastoid cells are usually well pneumatized, there is an irregular sclerosis, condensation and thickening of the promontory area in the region of the "oval window," and one margin of the fenestra vestibuli projects over the area of the vestibule and may appear thickened.[9] The Guillen projection appears to be best suited for the study of otosclerosis, but a roentgenogram in the Chaussé III projection should also be obtained to demonstrate the region of the vestibule.

Case VI. B.J., a 36 year old female, was admitted to the hospital because of progressive loss of hearing over a period of 7 years. There was no history of past infection of the middle ear. The loss of hearing was confirmed by the audiogram.

Roentgenograms (Fig. 12, *A* and *B*) showed a normal attic wall and ossicles. In the region of the fenestra vestibuli, however, there was condensation and a bony reaction. There was also condensation of the fenestra vestibuli projecting into the vestibule. A roentgenologic diagnosis was made.

Surgery was carried out on the left side which was less severely involved. The stapes was removed and the diagnosis of otosclerosis confirmed.

Case VII. B.V.P., a 36 year old female, was admitted because of bilateral gross loss of hearing of 20 years' duration, which was confirmed by an audiogram. There was no history of infection in either ear.

Roentgenograms (Fig. 13, *A* and *B*) showed a normal attic wall and ossicles. A thickened edge of the fenestra vestibuli which projected into the vestibule was noted. There was also irregular condensation and bone formation in the fenestra vestibuli.

At surgery the right stapes was removed and an area of marked sclerosis was noted around the "oval window." This confirmed the roentgenologic impression.

←

Fig. 10. Case V. Cholesteatoma of the antral area with fistula of the lateral semicircular canal. (*A*) Chaussé III projection. (*B*) Diagram of *A*. (1) Irregular and sclerotic attic wall; (2) complete destruction of the ossicles; (3) enlarged and oval antral area; (5) fistula of the lateral semicircular canal. (*C*) Guillen projection. (*D*) Diagram of *C*. Same findings as in *B*.

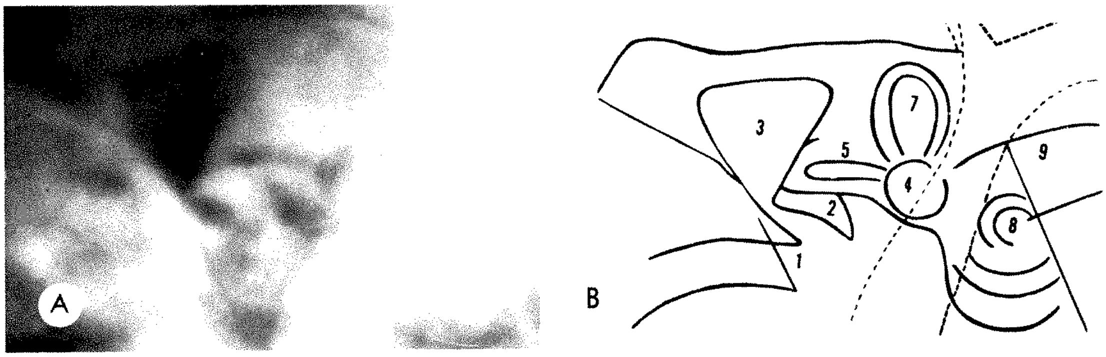


Fig. 11. Large epitympanic recess. (*A*) Chaussé III projection. (*B*) Diagram of *A*. (1 and 2) Normal appearance of the attic wall and ossicles; (3) large epitympanic recess and antral area.

Comment. The differential diagnosis in these cases should include inflammatory reaction in the area of the fenestra vestibuli, where a thickened margin might be found.

Congenital malformations. Our technique has also been of value in the study of congenital malformations of the ear as, for example, in the case of a deformed or absent stapes. A thickened foot plate or narrow middle ear may be demonstrated. Anomalies of the lateral semicircular canal can also be visualized.

Case VIII. H.R., a 13 year old patient, was admitted to the hospital for a congenital malformation of both auricles. There was agenesis of the auricle and of the external auditory meatus and canal on the right. On the left, agenesis of the auricle was also present, but the external canal was well developed. Conduction type loss of hearing was demonstrated on the left.

Roentgenograms (Fig. 14, *A* and *B*) of the right side showed malformation of the attic wall and of the middle ear. The ossicles were also abnormally shaped.

At surgery a small flat bone measuring 0.5 ×0.4 cm. was found. Its morphology did not conform to that of ear ossicles. No fenestra vestibuli or fenestra cochleae was found.

Trauma and postoperative follow-up. Other uses for the described projections would be in cases where trauma to the petrous portions is suspected[7,18] and also following mastoidectomy as a basis for comparison, should a cholesteatoma reoccur.

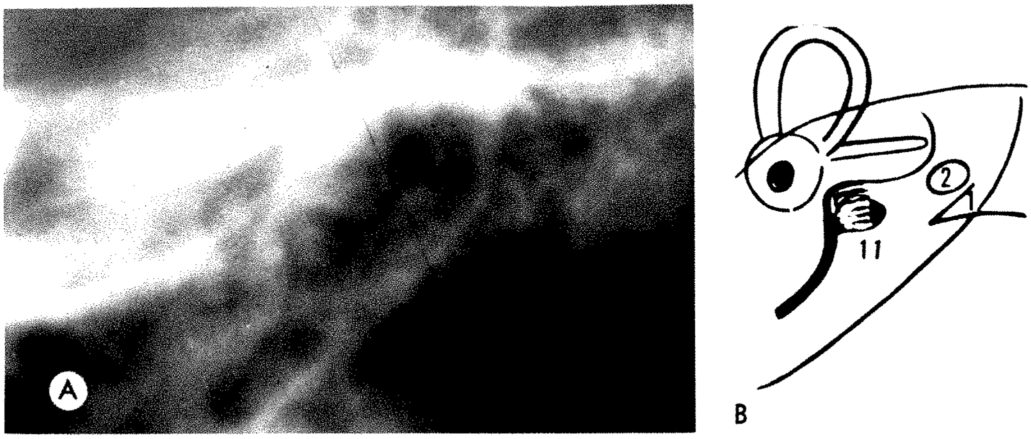


Fig. 12. Case VI. Otosclerosis. (*A*) Guillen projection. (*B*) Diagram of *A*. (1 and 2) Normal appearance of the attic wall and ossicles; (11) condensation and bony reaction in the area of fenestra vestibuli projecting into the vestibule.

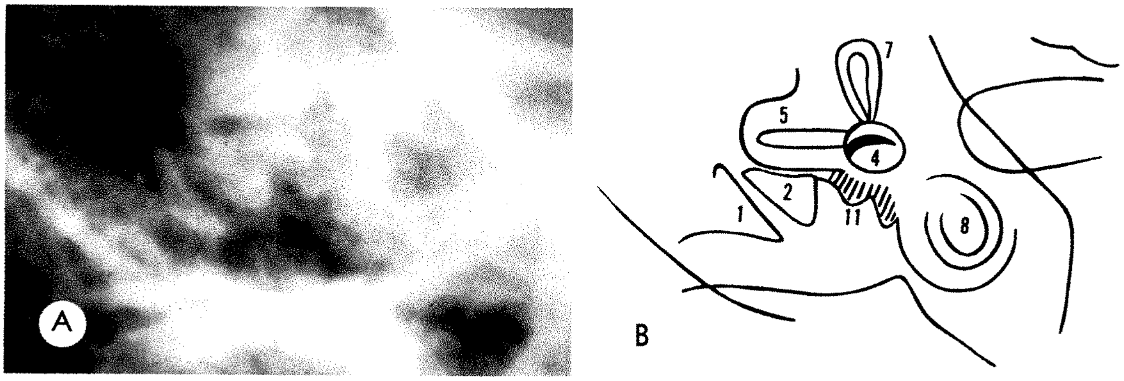


Fig. 13. Case vii. Otosclerosis. (*A*) Chaussé iii projection. (*B*) Diagram of *A*. (4) Thickened lip of the fenestra vestibuli projecting into the vestibule; (11) irregular condensation and bone formation in fenestra vestibuli; (12) normal attic wall and ossicles.

SUMMARY

1. A roentgenographic technique is described in which use is made of 3 projections for study of the middle ear and antral regions.

2. The results obtained by the combined Chaussé iii and Guillen projections in diagnosing cholesteatoma of the attic, adital and antral regions prior to surgery were found to be superior to those reported when only the Chaussé iii projection was used.

3. The roentgenographic features of cholesteatoma of the attic wall are irregularity, blurring and sclerosis of the attic wall; erosion of its apical or supra-retrotympanic portion; erosion of the posterior part of the external meatus; a blurred interspace between the attic wall and the ossicles; and haziness extending to the eustachian tube.

4. The roentgenographic features of cholesteatoma of the adital region are sclerosis, haziness and partial or complete destruction of the ossicles; an abnormal clear space between the ossicles and the lateral semicircular canal; adital widening with or without sclerosis; nonvisualization or poor visualization of the epitympanic recess; and blurred fenestra vestibuli.

5. The roentgenographic features of cholesteatoma of the antral region are a clear oval defect as small as 6×4 mm. in the antral area, with a well circumscribed clearly defined outline and an eroded lateral semicircular canal. Fistulas are easily visualized.

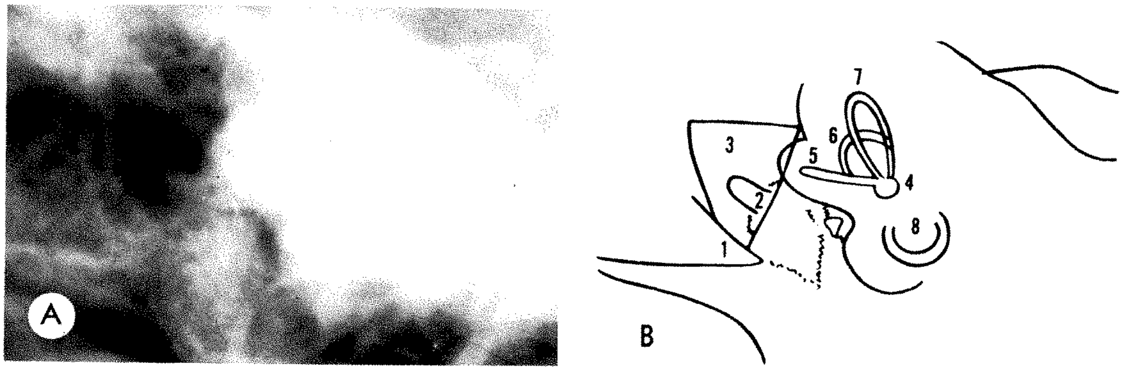


Fig. 14. Case viii. Malformation of the right middle ear. (*A*) Guillen projection. (*B*) Diagram of *A*. (1) Malformed attic wall; (2) abnormal shape of the ossicles (disclosed surgically); (11) haziness of the middle ear which was also malformed.

6. The use of these projections is also of value in the study of otosclerosis, congenital malformations and trauma to the petrous portions of the ear, as well as for postoperative follow-up.

Department of Radiology
Hôpital Maisonneuve
5415 Boulevard de l'Assomption
Montréal 36, Québec, Canada

The author gratefully acknowledges the collaboration of Dr. A. Arsenault, Chief, and Dr. R. Thibert, Assistant, of the Department of Oto-Rhino-Laryngology of l'Hôpital Maisonneuve, and also thanks Mr. Gauthier of the Medical Photography Service of l'Hôpital Maisonneuve, who carefully carried out the difficult assignment of reproducing the original roentgenograms for publication.

REFERENCES

1. Antoine, A., Grimard, R., and Wayoff, M. Fausses images de cholestéatome. *J. de radiol., d'électrol. et de méd. nucléaire*, 1958, *39*, 167–168.
2. Biessy, R. Contribution à l'étude radiologique des otorrhées chroniques. Thèse Diplôme de Lyon, 1959.
3. Brünner, S., Petersen, O., and Stoksted, P. Tomography of auditory ossicles. *Acta radiol.*, 1961, *56*, 20–29.
4. Chaussé, C. Trois incidences pour l'examen du rocher. *Acta radiol.*, 1950, *34*, 274–287.
5. Chiat, H., and Kittredge, R. D. Cholesteatoma of temporal bone. *Radiology*, 1958, *71*, 559–562.
6. François, J., and Barrois, J. Anatomie tomographique de l'os temporal normal. *Ann. radiol.*, 1959, *2*, 71–98.
7. Gros, C., Walter, J.-P., Block, J., and Bourjat, P. La paroi labyrintique normale. *J. de radiol., d'électrol. et de méd. nucléaire*, 1962, *43*, 253–258.
8. Guillen, G. Quelques apports aux techniques radio-otologiques modernes; l'incidence transorbitaire; la tomographie. *Rev. laryng.*, 1955, *76*, 395–446.
9. Guillen, G. Personal communication.
10. Jensen, G., Jespersen, C., and Brünner, S. Value of different projections in diagnosing cholesteatoma. *Acta radiol.*, 1960, *54*, 177–185.
11. Juster, M., and Fischgold, H. Étude radio-anatomique de l'os temporal. Masson et Cie, Paris, 1955.
12. Lemahieu, S. F. Valeur respective de l'incidence III de Chaussé et de la tomographie dans l'étude radiologique du rocher. *Acta oto-rhino-laryng. belg.*, 1952, *6*, 463–469.
13. Owen, G. R. Key area (attic-aditus-antrum) in chronic mastoid. *Tr. Am. Otol. Soc.*, 1951, *39*, 189.
14. Pendergrass, E. P., Hodes, P. J., Tondreau, R. L., and Marden, P. A. Tympanic cavity and auditory ossicles; roentgen findings in health and disease. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1956, *76*, 327–342.
15. Perras, P. Personal communication.
16. Portmann, M., and Guillen, G. Radiodiagnostic en otologie. Masson et Cie, Paris, 1959.
17. Roussel, J. Cliniques radiologiques. Masson et Cie, Paris, 1959, pp. 70–90.
18. Runström, G. On roentgen diagnostics of ear; technique and results. *Acta radiol.*, 1935, *16*, 630–632.
19. Samuel, E. Clinical Radiology of the Ear, Nose, and Throat. Paul B. Hoeber, New York; H. K. Lewis & Company, London, 1952.
20. Tarp, O. Tomography of temporal bone with Polytome. *Acta radiol.*, 1959, *51*, 105–116.
21. Wackeihem, A. Neuroradiologie. Doin et Cie, Paris, 1960.
22. Waltner, J. G. Roentgen diagnosis of cholesteatoma of middle ear. Am. J. Roentgenol. & Rad. Therapy, 1949, *62*, 674–684.
23. Wangermez, C., Portmann, M., and Guillen, G. Le radiodiagnostic en O.-R.-L.; présentation du cranio-tomographe universel du Dr. Guillen. *J. de radiol., d'électrol. et de méd. nucléaire*, 1957, *38*, 277–230.
24. Wayoff, M., Tenenbaum, J., and Tenenbaum, P. Fistule de canal semi-circulaire externe objectivée par la radiographie. *J. de radiol., d'électrol. et de méd. nucléaire*, 1958, *39*, 183–184.
25. Winderen, L., and Zimmer, J. Cholesteatoma of middle ear. *Acta radiol.*, 1954, Suppl. 111.

PITUITARY INSUFFICIENCY FOLLOWING MENINGITIS*

REPORT OF A CASE WITH ROENTGENOGRAPHIC SIGNS SIMULATING OSTEOPOROSIS CIRCUMSCRIPTA

By DONALD G. WETHERBEE, M.D.,† *and* JOHN W. TURNER, M.D.‡
SPRINGFIELD, MASSACHUSETTS

PITUITARY insufficiency is usually the consequence of intra- or supra-sellar tumor or of infarction of the gland, the latter most commonly occurring as a post-partum complication (Sheehan's syndrome). However, a wide variety of processes has been reported from time to time to cause anterior pituitary destruction, and we wish to add a case in which purulent meningitis led to Simmonds' disease and eventual death from coronary occlusion. Demonstration on roentgenograms early in the course of the disease of unusual changes in the skull, showing possible sellar enlargement and an area of apparent osteoporosis circumscripta, constituted remarkable concomitant findings.

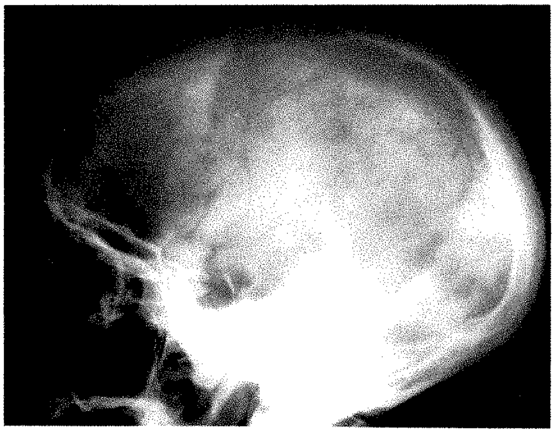


FIG. 1. March 7, 1955: Lateral skull roentgenogram showing thin decalcified posterior clinoid processes and a sharply defined radiolucent alteration roughly equal to the right parietal bone.

REPORT OF A CASE

A 38 year old male police officer, who had always been in good health, was hospitalized March 5, 1955 after 2 days of fever, severe headache and vomiting which had not been noticeably affected by tetracycline. He was disoriented and stuporous, had a temperature of 103°F., blood pressure of 105/60 and pulse of 64 accompanied by a stiff neck, but no localizing neurologic signs. The cerebrospinal fluid was under increased pressure and contained 6,700 cells per cubic mm., almost all of which were polymorphonuclear leukocytes. Cerebrospinal fluid protein was 100 mg. per 100 ml., sugar 37 mg., and chlorides 116 mEq./L. No definite organisms were identified on stained slides, and culture of the spinal fluid produced no growth, probably reflecting the previous antibiotic therapy. On March 7, roentgen study of the chest showed no disease. The posterior clinoid processes were found on lateral skull roentgenograms to be thin and elongated (Fig. 1) and a zone of decalcification roughly equivalent to the right parietal bone was thought suggestive of osteoporosis circumscripta. The presumption of bacterial meningitis seemed inescapable, despite the failure to demonstrate a specific organism, and the patient was treated with sulfadiazine, penicillin and streptomycin.

He steadily improved, but by the fifth hospital day complained of blurred vision. When on the seventh day he could cooperate sufficiently, large defects involving the temporal halves of the left and right visual fields could be outlined roughly by confrontation. By the fourteenth day, the right visual field appeared to have expanded virtually to normal, but the left temporal defect cleared more slowly. Antibiotics were discontinued by the twelfth day. An ophthalmologist confirmed the left visual field defect by perimetry study before the patient's discharge on the seventeenth day, but

---

* From the Departments of Internal Medicine and Radiology, Wesson Memorial Hospital.
† Internist, Medical Staff, Wesson Memorial Hospital.
‡ Radiologist, Wesson Memorial Hospital.

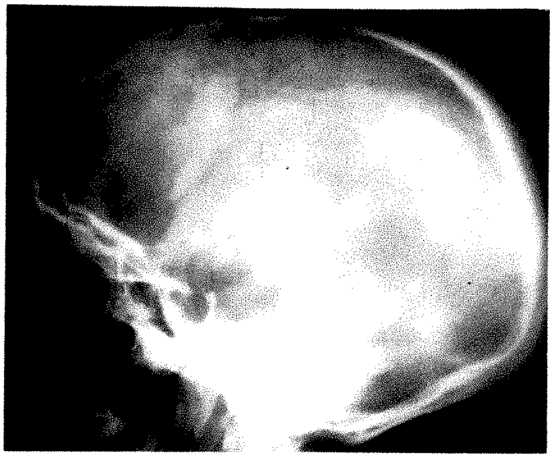


FIG. 2. September 14, 1961: Recalcification of the sella turcica and the right parietal bone after 6½ years.

found both fields normal on re-examination in May, 1955. Soon afterwards the patient returned to work, evidently in restored health.

In April, 1957 he hurt his back in an automobile accident. The injury did not respond to conservative treatment, and he was again hospitalized on December 16, 1958. The only physical abnormalities were hypalgesia over the left L4 dermatome and an absent left knee jerk. Myelograms showed disk protrusion between the third and fourth lumbar vertebrae, principally to the left of the midline. Excision of the disk and fusion of lumbosacral area, including L3 and L4 vertebrae, were done on January 2, 1959. He had a long and difficult postoperative course, complaining of weakness, lethargy and emotional depression and never returned to full-time duty as a police officer.

He was lost to follow-up between March, 1959 and September 11, 1961, when he was again hospitalized complaining of exhaustion and weakness in spite of sleeping many hours daily. During the previous year he had been impotent and without libido, had become increasingly intolerant of any but very warm environmental temperature, and had noticed a susceptibility to respiratory infections. Though his appetite was poor, he had gained 20 pounds in the preceding 4 months. For several months he had experienced episodes of substernal pain with radiation into the left arm, not necessarily related to exercise.

Physical examination showed him to be 70 inches tall, weighing 175 pounds. Blood pressure was 110/60, pulse 60. He was lethargic and slow of speech and had difficulty concentrating. His skin was sallow and he had a pudgy appearance. There was some puffiness about his eyes, and a trace of pitting edema of the lower legs. There was no abnormal pigmentation, but the axillary and chest hair was virtually absent and the pubic hair sparse. There was nothing else of note on the physical examination.

Laboratory data showed a hemoglobin of 11.4 gm. per cent, hematocrit of 31 mm. in 1 hr., white blood cell count of 6,400 with 49 per cent polymorphonuclear leukocytes, 47 per cent lymphocytes, 1 per cent monocytes, and 3 per cent eosinophils. Urinalysis was unremarkable. Fasting blood sugar was 94 mg. per cent, blood urea nitrogen 13.6 mg., serum cholesterol 400 mg., protein bound iodine 3.2 μg., total iodine 5.6 μg., and 17 hydroxycorticoids 4.9 mg./24 hr. Eosinophil count was 281, dropping to 83 six hours after 25 mg. ACTH intramuscularly. Radioactive iodine uptake was 14 per cent in 6 hours, 20 per cent in 24 hours; after 10 units of TSH, uptake after 3 hours was 22.5 per cent and at 24 hours 54 per cent. The electrocardiogram showed low voltage throughout,

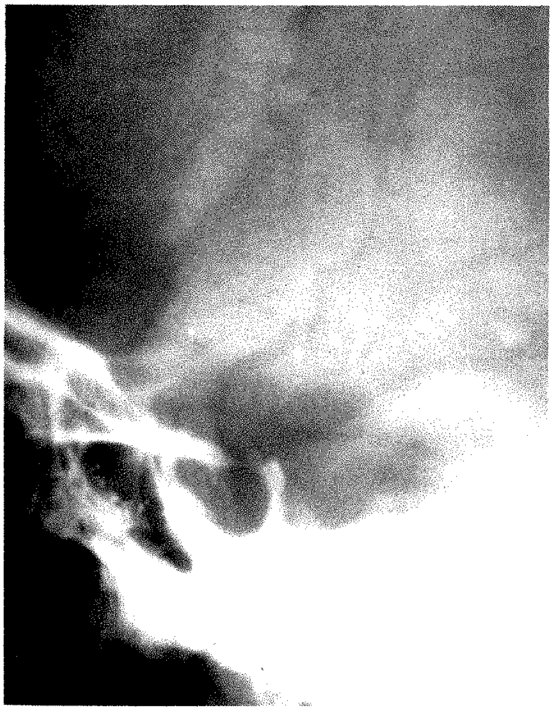


FIG. 3. September 14, 1961: Detail roentgenogram of the sella turcica showing restoration of posterior clinoids and increased calcification generally in the sellar area.

consistent with a hypothyroid state, and also T wave changes suggesting nonspecific myocardial damage. After an oral water load of 1,500 ml., urine output was only 200 ml. in 12 hours, a response highly suggestive of adrenal cortical insufficiency. Skull roentgenograms (Fig. 2 and 3) showed that recalcification of the sella turcica and of the right parietal bone had occurred in the interval of 6½ years.

At this point in the study, the patient requested discharge. Therefore, on September 23 cortisone 5 mg. daily was begun and he was given 100 mg. testosterone propionate intramuscularly. Thyroid hormone was withheld at the outset for fear of precipitating an adrenal crisis. Cortisone was increased by increments until late in October at which time a dose of 50 mg. daily had been reached. On October 15, he was started on ¼ grain thyroid daily, and this was increased a week later to ½ grain. On October 28, he received an additional 100 mg. of testosterone propionate.

He continued to complain of mild substernal pain with radiation into his left arm, though of no greater severity or duration than before, but on the evening of October 30, he had an attack of similar but much more severe pain which lasted through the night. He was readmitted to the hospital on October 31, obtained relief of pain for some hours, but expired abruptly on the following morning.

Autopsy demonstrated extensive atheromatous deposits in the aorta and coronary arteries, with recent thrombosis of the left anterior descending artery. The pituitary gland was small, soft and surrounded by adhesions; microscopically the gland consisted mostly of hyalinized connective tissue with residual islands of pituitary cells. These findings were interpreted by the pathologist as consistent with old infarction. Sections of the thyroid revealed atrophic small acini containing thin colloid and an increase in connective tissue throughout. The adrenal cortex was extremely thin, six or seven cell layers, with little evidence of activity. There appeared to be maturation arrest of spermatozoa in the testicular tubules and a slight increase in connective tissue; no Leydig cells could be identified.

DISCUSSION

In some cases of pituitary insufficiency, the gland at autopsy shows long-standing scarring, fibrosis and atrophy, and it is often difficult or impossible to uncover the original disease.[3] However, the localization in this instance of an inflammatory process close to the pituitary gland, signaled by the involvement of the optic chiasm early in the course of the disease, implicates the basal meningitis as the cause of early infarction and cellular destruction with subsequent fibrous replacement.

The interval between the insult to the pituitary gland and the appearance of symptoms of target organ deficiencies may be brief or delayed for years.[1] The patient's slow convalescence from the disk operation probably signified that hormonal deficiencies were by then present but unrecognized. The operation may also have further increased adrenal cortical stress to the point where inadequacy of adrenal cortical function became clinically manifest.

Roentgenologically, the right parietal and sellar recalcification suggested that all bone changes were related to the infection. The infection, in turn, was, no doubt, controlled by the antibiotics. This is an unusual example of cranial recalcification. There was no evidence of Paget's disease clinically or at postmortem examination. The pantopaque globules noted on the final skull roentgenograms may have had some influence on the iodine 131 uptake, but the response to thyroid stimulating hormone of 34 per cent increase in 24 hours coincides rather closely with an average increase of 32.2 per cent recorded on comparative iodine 131 uptakes by Perloff *et al.*[2] after TSH administration in patients with pituitary hypothyroidism. They found elevations by TSH administration to be only 7.6 per cent in patients exhibiting primary hypothyroidism and 20.8 per cent in euthyroid patients given this test.[2]

The serum cholesterol level is most often normal or subnormal in secondary as contrasted with primary hypothyroidism, though markedly elevated levels may sometimes be present.[4] It is possible to reason, but not to establish conclusively that coronary atheromatosis and death from coronary occlusion at this relatively early age was directly if remotely related to the meningitis by way of pituitary insufficiency through hypothyroidism and hypercholesterolemia.

SUMMARY

A case of pituitary insufficiency following meningitis, with eventual death from coronary occlusion is presented.

Unusual changes simulating osteoporosis circumscripta are described and demonstrated on skull roentgenograms.

John W. Turner, M.D.
Wesson Memorial Hospital
Springfield 01105, Massachusetts

REFERENCES

1. FARQUHARSON, R. F. Simmonds' Disease: Extreme Insufficiency of the Adenohypophysis. (A monograph in the American Lecture Series). Charles C Thomas, Publisher, Springfield, Ill., 1950.
2. PERLOFF, W. H., LEVY, L. M., and DESPOPOULOS, A. Use of thyrotropic hormone (TSH) in diagnosis of myxedema. *J. Clin. Endocrinol.*, 1951, *11*, 1495–1502.
3. SHEEHAN, H. L., and SUMMERS, V. K. Syndrome of hypopituitarism. *Quart. J. Med.*, 1949, *18*, 319–378.
4. WILLIAMS, R. H., Editor. Textbook of Endocrinology. Second edition. W. B. Saunders Company, Philadelphia, 1955.

TRAUMATIC PNEUMOCEPHALUS*

By ROBERT J. KAHN, M.D.,† *and* ALVIN L. DAYWITT, M.D.
DENVER, COLORADO

OUR location in a moderate sized city, with a great drawing area of medical problems, allows us to survey many cases of head injury. Considering this, we have found the occurrence of traumatic pneumocephalus a fairly rare occurrence. In the past 13 years 3 cases of this entity have been observed in this hospital. We feel that the relative sparsity of such cases, the dramatic roentgen findings that may be seen, and the possibility of serious complications warrant our reporting the following cases.

REPORT OF CASES

Case 1. A 48 year old white male sustained severe injuries after falling into a hole, 7 feet deep, landing on his feet, and then hitting his head on a hard surface. Lacerations were sutured at another hospital, and the patient was transferred to our hospital for further evaluation because of blurred vision and changes in sensorium. Physical examination on admission revealed a blood pressure of 120/90, pulse 104 and regular. The pupils were round, regular and equal and reacted to light and accommodation. Funduscopic and neurologic examination was normal. Skull roentgenograms (Fig. 1, *A* and *B*) obtained 6 hours after the accident revealed a comminuted fracture of the frontal bone which extended into the ethmoid cell group and also involved the frontal sinus. The most remarkable finding on the skull roentgenograms was the presence of a large collection of subdural air, and good filling of both lateral ventricles, and a minimal amount of subarachnoid air.

The patient's hospital course was essentially uneventful for approximately 8 days. He was treated conservatively, with bed rest and antibiotics, with gradual clearing of his sensorium. The patient remained afebrile on this regimen, and on the eighth hospital day his antibiotic therapy was discontinued. Approximately 6 hours after discontinuing the antibiotic therapy, the patient became febrile and developed nuchal rigidity. Lumbar puncture performed at this time revealed xanthochromic fluid, 7,600 white blood cells per cubic centimeter with a differential count of 75 per cent polymorphonuclear neutrophils and 26 per cent lymphocytes;

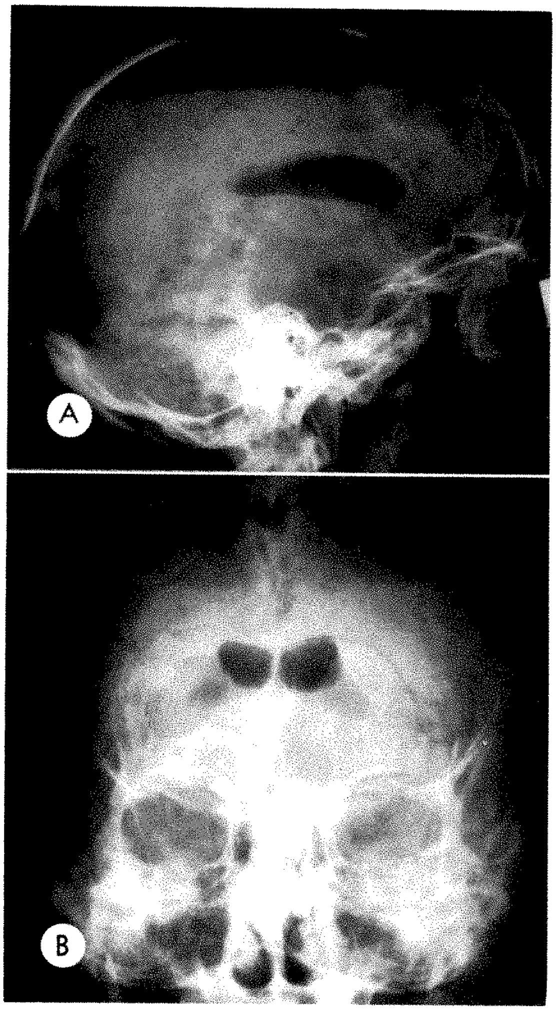


Fig. 1. Case 1. (*A* and *B*) Skull roentgenograms demonstrating a comminuted fracture in the frontal region, involving the frontal sinus and probably extending into the ethmoid. The air is primarily subdural and intraventricular.

---

* From the Department of Radiology, Veterans Administration Hospital, Denver, Colorado.
† Now at General Rose Memorial Hospital, Denver, Colorado.

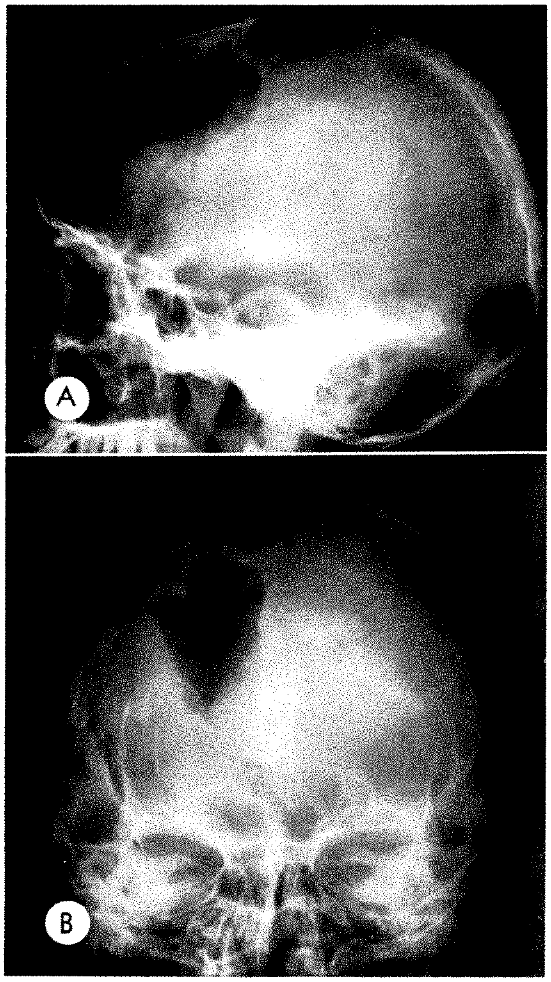


FIG. 2. Case II. (*A* and *B*) Frontal fracture extending into the frontal sinus. Moderately large collection of air is apparently localized to one side and is probably intracerebral. There is no definite evidence of intraventricular or subdural air.

450,000 red blood cells per cubic centimeter were present. Antibiotics were then reinstituted and the patient became afebrile 6 days after this episode. A repeat lumbar puncture 18 days after admission, and approximately 10 days after the first lumbar puncture, revealed only 130 red blood cells per cubic centimeter, 25 white blood cells, with a differential of 25 per cent polymorphonuclear neutrophils and 75 per cent lymphocytes. Roentgenographic reexamination of the skull 11 days after the initial injury demonstrated that air was no longer present in the subdural space. Ventricular air was still present but was diminished. Repeat examination at 21 days revealed the complete disappearance of air within the cranial vault. The patient remained afebrile, never showed any evidence of cerebral spinal fluid rhinorrhea, and was finally discharged on the twenty-third hospital day, without further treatment.

CASE II. A 33 year old Spanish-American male was admitted to this hospital approximately 6 weeks after a serious automobile accident, in which he sustained multiple fractures of the skull and face. He was initially admitted to another hospital. After 1 month he had only occasional right sided headaches and was discharged from that hospital. The patient was then re-admitted approximately 1 week later because of dizziness, lethargy and difficulty in concentrating. Roentgenograms at this time showed air in the cranial vault, and the patient also had rhinorrhea. In essence there was approximately a 5 week interval between the time of the accident and the appearance of roentgenographically detectable intracranial air. At the time of these findings, the patient was transferred to this hospital for further study. Physical examination revealed slurred speech. The patient's right optic disk was pale and there was blindness of the right eye. There was diminished hearing acuity in the right ear. Rhinorrhea was observed from the right nostril. Roentgenograms showed multiple linear skull fractures involving the left frontal region and the superior and lateral portions of the left orbit extending into the greater wing of the sphenoid (Fig. 2, *A* and *B*). A large collection of air was seen overlying the right frontal lobe. The air was intracerebral in location. No evidence of intraventricular air was noted. A repeat examination of the skull 1 week later showed that the amount of pneumocephalus was reduced to approximately 40 per cent. However, the brain was not entirely clear of air until 8 to 9 weeks after admission to this hospital, which would be approximately 14 weeks after the initial injury. When the patient was discharged, there was still felt to be a degree of mental confusion, and the patient has never been able to return to his normal daily activities.

CASE III. The complete clinical record was not available on this patient; however, he had a serious accident and was unconscious several days. Roentgenograms of the skull revealed a moderate amount of air in both lateral ventricles. A severe comminuted and depressed fracture of the frontal region was also noted (Fig. 3, *A* and *B*). We know only of the permanent effects in this patient. He complained of blindness in the left eye, anosmia, depression, and dizziness which made him physically unable to work.

DISCUSSION

In 1913, Luckett[4] first described the finding of air in the ventricles of the brain following trauma. Since that time there have been sporadic reports of similar nature, but Luckett's case was one of the most vividly described. Another single occurrence was reported in 1918.[3] A case presented in 1919 was of particular interest because of visualization fluoroscopically of an audible succussion splash in a patient who was found to have post-traumatic subdural and ventricular air.[7]

Traumatic pneumocephalus is a fairly rare consequence of skull injuries; however, there have been several large series of head injuries reported with this finding. One such series presented 65 cases, of which 24 showed some type of traumatic pneumocephalus.[5] Another group included 22 cases of traumatic pneumocephalus, exclusive of penetrating gunshot wound.[1]

Classification of pneumocephalus on an etiologic basis can be simply divided into three categories: traumatic, nontraumatic, and diagnostic. In this paper we concern ourselves principally with the traumatic type. Nontraumatic types are usually caused by erosions due to tumor or infection. Osteomas of the ethmoid sinus and cholesteatomas secondary to chronic otitis media have been incriminated in this process. Traumatic pneumocephalus may be subdivided into several types according to its anatomic location. These can be recognized only by roentgen methods. The findings are: (1) extradural air. In this type there is usually only a small amount of fixed air present; (2) subdural air. This is usually a larger amount of air, which shifts with different positions of the patient and often shows an air fluid level; (3) subarachnoid air. The features are similar to diagnostic pneumoencephalograms. Usually this air enters the ventricles through the foramina of the fourth ventricle, but rarely there may be a direct tear into a lateral ventricle; and (4) intracerebral air. This is most often seen extending upwards from the floor of the anterior fossa and is most often unilateral. No fluid level is seen, and the air does not shift with positioning of the patient.

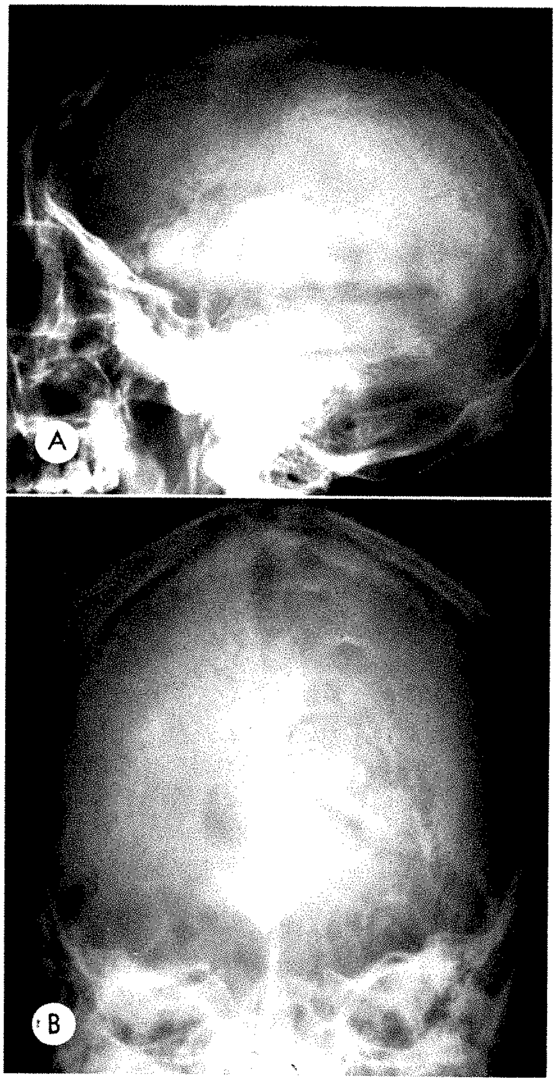


Fig. 3. Case III. (*A* and *B*) Comminuted depressed fracture of the frontal region with a minimal amount of air in the ventricles. No significant subdural or subarachnoid air is visualized.

Whenever pneumocephalus exists after trauma, a fracture must be present, even though at times the fracture may not be evident. When a fracture occurs through one of the air-containing cavities of the skull, pneumocephalus may be produced.

The mechanism of this air transfer is most probably due to simple pressure relationships.[2] Increased pressure secondary to coughing or sneezing may force air into the ventricles. The pathway of air may be from the area of dural tear to the subarachnoid basilar cisterns. From this location the air may then enter the fourth ventricle through the medial and lateral foramina, then through the aqueduct of Sylvius into the third ventricle, into the lateral ventricles through the foramen of Monro, then spread into each lateral ventricle through the interventricular foramina. Thus, in essence, the air follows the anatomic pathway of the cerebral spinal fluid.

Pneumocephalus may manifest itself within varying lapses of time. In the large series of 22 cases,[1] 15 showed some type of intracranial air within 4 days following injury. In the remaining 7 cases, no gas was seen on first examination, but was eventually found 1 to 6 weeks after injury. A more recent case,[9] presented interesting facets of this entity. The patient had a serious accident, with resultant trauma about the head. His hospital course for 18 days was precarious. The initial roentgenograms showed a nasal fracture, and another area in the skull was questionable for fracture. No air was seen in the cranial vault at this examination. The patient was finally discharged, and after several days developed headache, nausea, and eventually became comatose. He was re-admitted and this time roentgenograms revealed a fracture through the frontal sinus and the presence of intracranial air. The clinical impression from laboratory work and physical examination was that the patient had meningitis. On further investigation of the patient's history, it was noted that he had developed a head cold on discharge from the hospital, and these progressive symptoms developed after excessive nose blowing.

Meningitis may be an early or a late complication secondary to a fracture where pneumocephalus is noted. If the dural tear closes spontaneously, there is usually an orderly sequence noted in the follow-up roentgenograms. This has been reported previously;[8] 10 days after the appearance of intracranial air was noted, the subdural air was absorbed, and the ventricular air was still present but diminished. Nineteen days after the initial discovery, the ventricular air was no longer visible. In our Case I, subdural air was absent 11 days after discovery, and ventricular air was no longer present after 21 days. Although complications must always be guarded against, the period of active prophylactic treatment may be terminated after there is good evidence of resorption of most of the air. As can be noted by Case I, the rapidity of development of symptomatic meningitis on the seventh day after trauma, several hours after cessation of active antibiotic therapy, was alarming. After reinstitution of antibiotic treatment, the patient soon again became asymptomatic, and on withdrawal of the antibiotics on the eighteenth day the patient remained asymptomatic. In diagnostic pneumocephalograms in uncomplicated cases, complete air resorption can be noted within 2 to 12 days.[6] Obviously, many of the sequelae seen in such patients are due to the direct effect of the injury, either on the cranial nerves or on the central nervous system appendages about the head. The possible sequelae and complications due to direct effects of trauma were probably the major cause of the permanent difficulties incurred by Case II and Case III in our series. It cannot be stressed too often that the most dreaded complication seen in patients having traumatic pneumocephalus is that of meningitis. Whenever air persists longer than 3 to 4 weeks, the incidence of meningitis may be increased. It may then be impractical as well as dangerous to continue conservative treatment, and surgical repair of the dural defect seems advisable. Even with normal resorption of the air, one cannot be certain that late complications may not occur. In a reported case of a 5 year old girl with a petrous fracture with mastoid involvement,[5] meningitis developed 9 years later, one day after onset of acute otitis media. This rapid onset of meningitis after such a short duration of otitis media was suspicious of some underlying process which hastened the development of intracranial infection. Surgery was performed, and a 5 mm. defect in the dura was repaired.

SUMMARY

By presenting our cases and other cases described in the literature, we have attempted to emphasize that traumatic pneumocephalus is not only an interesting roentgenographic finding, but that it is a manifestation of injury that may be likened to compound fracture anywhere else in the body. Meningitis as a serious complication of this type of injury is stressed. The finding of pneumocephalus after trauma for the reasons stated above affects the prognosis of the patient.

Robert J. Kahn, M.D.
General Rose Memorial Hospital
1050 Clermont Street
Denver 20, Colorado

REFERENCES

1. Eaglesham, D. C. Radiological aspects of intracranial pneumocephalus. *Brit. J. Radiol.*, 1945, *18*, 335–343.
2. Gassmann, W. Traumatische Pneumatozele. *Zentralbl. Chir.*, 1957, *82*, 2130–2133.
3. Holmes, G. W. Intracranial aerocele following fracture of frontal bone: with report of case. Am. J. Roentgenol., 1918, *5*, 384–386.
4. Luckett, W. H. Air in ventricles of brain, following fracture of skull. *Surg., Gynec. & Obst.*, 1913, *17*, 237–240.
5. Morley, T. P., and Hetherington, R. F. Traumatic cerebral spinal fluid, rhinorrhea and otorrhea, pneumocephalus and meningitis. *Surg., Gynec. & Obst.*, 1957, *104*, 88–98.
6. Pendergrass, E. P., Schaeffer, J. P., and Hodes, P. J. The Head and Neck in Roentgen Diagnosis. Charles C Thomas, Publisher, Springfield, Ill., 1956, p. 1261.
7. Potter, H. E. Case of hydro-pneumo-cranium, with air in ventricles. Am. J. Roentgenol., 1919, *6*, 12–16.
8. Storm-Mathisen, A. Traumatic pneumocrania and subdural spinal fluid. *Neurology*, 1954, *4*, 78–82.
9. Thum, H. J. Pneumocephalus nach nicht erkanntem Schädelbruch. *Monatsschr. Unfallh.*, 1959, *62*, 14–18.

THE VENTRICULAR SPAN IN CEREBRAL PNEUMOGRAPHY*

By H. JOACHIM BURHENNE, M.D., SAN FRANCISCO, CALIFORNIA, *and* HUGH DAVIES, D.M. (OXFORD), LONDON, ENGLAND

RADIOLOGIC pneumography remains the only method by which the cerebral ventricular system can be made visible and be measured *in vivo*. No acceptable conclusion is permissible, however, concerning the amount of ventricular fluid volume, as adequate quantitative studies correlating neuroradiologic and anatomico-pathologic findings are not available. In interpreting cerebral air studies, the radiologist must decide whether the ventricles are normal or dilated. This differentiation is especially difficult since anatomic studies concerning the normal fluid content of the cerebral ventricular system and its physiologic dilatation with advancing age are scarce in the medical literature.

Is there a single and practicable pneumoencephalographic measurement available which indicates ventricular enlargement?

Bruijn[1] correlated the volume of the ventricular system with the measurement of the maximal breadth of both lateral ventricles at the plane of the cellae mediae. He showed by statistical analysis of data in 103 cases that a rectilinear relation exists between ventricular size and width. The measure of spread of the lateral bodies includes the septum pellucidum and is obtained in the brow-up view (Fig. 1).

Utilizing this measurement, which we shall call the "ventricular span" (VS), the present study attempts to answer the following questions:

1. What is the normal range of the VS?
2. Does this single measurement reflect the size of the cerebral ventricular system?
3. To what degree does the ventricular apparatus increase with advancing age?
4. Is this physiologic dilatation large enough to prohibit the use of a radiographic measurement for all ages?
5. What is the range of the VS in general brain atrophy?
6. What diseases are associated with an increased VS that is not due to obstruction?
7. What is the incidence of normal ventricular asymmetry?

MATERIAL AND METHOD

First, 1,000 cerebral air studies were selected. This material consisted of an even number of cases with the radiologic diagnosis of normal and dilated ventricular systems. Sex, age, VS, width of the third ventricle, appearance of sulci and cisterns, and asymmetry of anterior horns and cellae mediae were listed. Finally, the clinical diagnosis on discharge, follow-up visits, or readmission were recorded. All roentgenograms were obtained in the same department from 1954 to 1960 by means of fractional pneumography on a Schönander table with a target film distance of 70 cm.

Not included in the study were patients in whom (a) inadequate filling did not permit visualization of the bodies of the lateral ventricles; (b) the brow-up view did not conform to the Frankfurt horizontale; (c) the ventricular dilatation was localized, not general; and (d) the ventricular asymmetry exceeded 5 mm.

The 1,000 cases were separated into two groups: Group A consisted of 500 patients with the radiologic diagnosis of a normal cerebral ventricular system. In the 500 in Group B, the radiologic diagnosis was generalized brain atrophy. Ventricular dilatation, without obstruction, was considered present in all cases.

---

* From the Radiological Department, The National Hospital for Nervous Diseases, Queen Square, London, England.

This study was supported by a special traineeship from the National Institute of Neurological Diseases and Blindness, U. S. Public Health Service.

RESULTS

GROUP A

The distribution of the VS measurements for 500 patients is represented in Figure 2. The measurements range from a minimum of 25 mm. to a maximum of 49 mm. Two standard deviations, or 95 per cent, include a range from 29 mm. to 45 mm. The arithmetical mean value is 37.5 mm. The sex distribution is 280 males and 220 females, and the average age 34.83 years.

Asymmetry of the lateral ventricles of not more than 5 mm. was present in 30 per cent of cases with a preponderance on the left at a ratio of 2.4:1.

Although the ventricular asymmetry was more pronounced in the anterior horns, in only 5 cases did this measurable difference not extend to the ventricular bodies.

GROUP B

Figure 3 shows the distribution of the VS measurements which range from a minimum of 40 mm. to a maximum of 91 mm. in 500 patients. The arithmetical mean value is 51 mm. The 500 patients comprise 349 males and 151 females with an average age of 50.36 years.

Asymmetry of the lateral ventricles measures not more than 5 mm. in 35 per cent of the cases, with a ratio of 2.5:1 preponderance on the left.

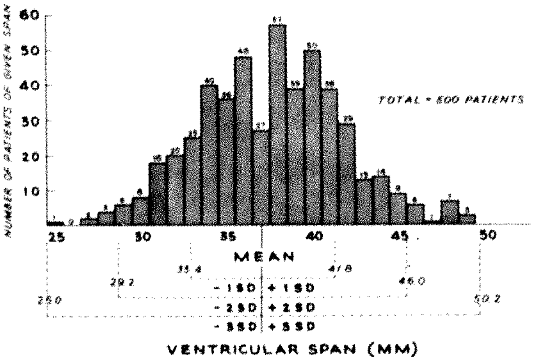


Fig. 2. Histogram of ventricular span in Group A. Distribution of ventricular span measurements in 500 patients with the radiologic diagnosis of a normal cerebral ventricular system.

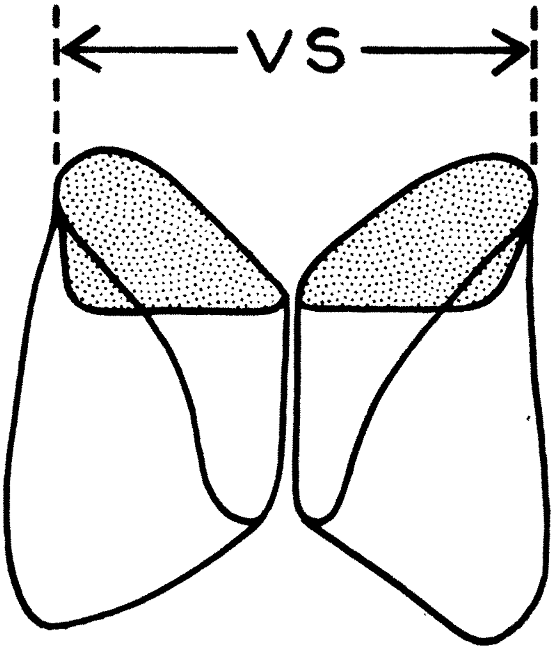


Fig. 1. The ventricular span is the measure of maximal spread of the lateral bodies. It is obtained in the brow-up view and includes the septum pellucidum.

ANALYSIS

Only the histogram for Group A compares favorably to an ideal curve of normal frequency distribution. The values for the mean, mode, and median coincide. Symmetrical distribution around the arithmetical mean is present. With a standard deviation of 4.2, our material in Group A compares with a normal frequency distribution as follows: 1 standard deviation = 68.5 per cent (ideal 68.27 per cent); 2 standard deviations = 95.40 per cent (ideal 95.45 per cent); and 3 standard deviations = 100 per cent (ideal 99.73 per cent).

The mean VS for males was 38 mm. versus a mean of 37.1 mm. in females.

The age distribution for both groups is given in Table 1. In Group A, the VS increases noticeably between the first and second decades and again between the fifth and sixth decades, whereas the changes in measurement are negligible in the age period from 10 to 49 years (Fig. 4).

Measurement of the third ventricle and

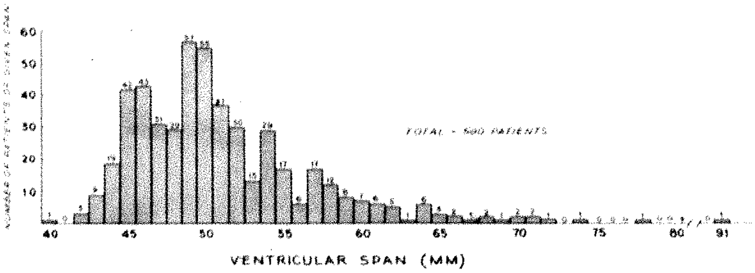


FIG. 3. Histogram of ventricular span in Group B. Distribution of ventricular span measurements in 500 patients with the radiologic diagnosis of generalized brain atrophy.

of the subarachnoid sulci over the cerebral convexity was considered as not being accurate or practical. The lateral limits of these structures are not well enough delineated on most roentgenograms to allow expression in millimeters. Enlargement of the third ventricle was thought to be present in 60 per cent of the 500 patients of Group B.

Hemisphere dominance was not taken into consideration, as it was not recorded in the records of every patient.

The final clinical diagnosis of the 1,000 patients of Group A and B are listed in Tables II and III.

Seventeen patients in Group A showed a VS of more than 45 mm. Their diagnoses are listed again in Table IV. Twenty-four per cent of these patients were demented, as compared with 3.5 per cent whose span measured less than 45 mm.

TABLE I

AGE DISTRIBUTION AND INCREASE IN VENTRICULAR SPAN IN 1,000 PATIENTS OF GROUPS A AND B

Age in Years	No. of Patients Group A	No. of Patients Group B	Arithmetical Mean Group A (mm.)	Ventricular Span Group B (mm.)
Birth to 9	21	23	36.04	52.00
10 to 19	98	23	37.14	51.30
20 to 29	74	17	37.37	49.35
30 to 39	107	39	37.29	49.92
40 to 49	89	67	37.74	51.28
50 to 59	79	157	38.50	50.37
60 to 69	31	149	38.64	51.65
70 to 79	0	23		51.39
80 to 89	1	2	48.00	50.00
Total	500	500		

Thirty-two patients in Group B, classified radiologically as having atrophy, showed a VS of less than 45 mm. In all but 5 (Table V) the normally well defined lateral angulation of the ventricular bodies was replaced by a characteristically blunt appearance with pronounced rounding of the lateral angle (Fig. 5, *A* and *B*).

Biopsy or necropsy was obtained in 30 patients of Group B. The findings are listed in Table VI. The diagnosis of brain atrophy was histologically confirmed in 16 of these patients of whom all but one were demented. No record concerning the mental status of this 2 year old child was available. Three of the 500 patients diagnosed by the radiologist as having atrophy are known to have had a glioma. Two brain tumors found at postmortem examinations had, in fact, been associated with general cerebral atrophy. The third tumor patient had not been

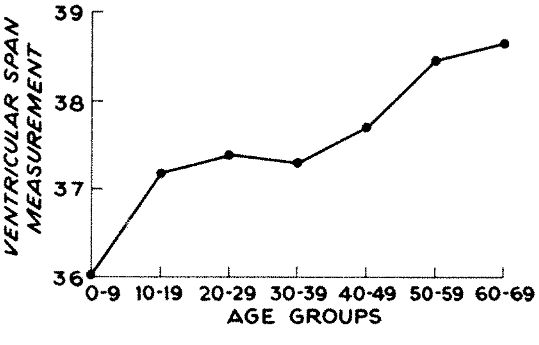


FIG. 4. Physiologic increase in ventricular span with aging.

demented and showed, on necropsy, no evidence of atrophy. All of 5 patients in whom a biopsy diagnosis was normal or inconclusive had dilated lateral ventricles on the roentgenograms and evidence of atrophy on surgical inspection of the brain surface, and all were demented.

DISCUSSION

In common with similar radiologic investigations of normal anatomy in the human, this study has the limitation that no large enough group of neurologically asymptomatic patients or of healthy volunteers is available for pneumoencephalographic measurements. The normal ventricular system can presently be assessed only by what the experienced neuroradiologist, who has seen a great number of air studies, considers not abnormal. Strictly speaking, we have expressed in figures what the radiologist at our institution regards as a normal or a dilated cerebral ventricular apparatus.

The statistical analysis of Group A, however, supports the assumption that we are studying a true sample of the population, namely the patient with a normal ventricular system. The curve of the histogram in Figure 2 corresponds with an ideal curve of a normal frequency distribution.

Another limitation lies in the application of measurements in practical radiology. Although they are of great help to the inexperienced, the measurements are no more than a guide for the well trained diagnostician in any given case. He considers size and configuration of each ventricle in conjunction with the appearance of sulci and cisterns to distinguish normal findings from atrophy.

It is of interest to evaluate at which measurement of the VS the radiologist drew the line in our study between these two conditions. If we incorporate the frequency distribution in Groups A and B (Fig. 2 and 3), we find, in general, a dividing line at the measurement of 44.5 mm. Thirty-two cases of Group B fall below this point and 17 of Group A above it. In our material of 1,000 cerebral air studies, 49, or 4.9 per cent, demonstrated a VS inconsistent with the 44.5 mm. measurement separating normal

Table II

FINAL CLINICAL DIAGNOSIS IN 500 PATIENTS WITH NORMAL VENTRICULAR AIR STUDIES. GROUP A

No abnormality	7
Headache	39
Migraine	11
Bell's palsy	1
Optic atrophy	6
Retrobulbar neuritis	11
Orbital pseudotumor	1
Proptosis	1
Labyrinthitis	2
Menière's disease	2
Conductive deafness	2
Benign intracranial hypertension	10
Toxic hydrocephalus	2
Hysteria	10
Anxiety neurosis	8
Psychosis	10
Ataxia	2
Little's disease	1
Perry-Romberg syndrome	1
Syringomyelia	1
Cerebellar degeneration	2
Metachromatic leukodystrophy	1
Multiple sclerosis	11
Parkinsonism	5
Narcolepsy	3
Epilepsy	211
Mental deficiency	11
Dementia	7
Dementia and brain atrophy	14
Meningitis	1
Encephalitis	6
Schilder's disease	1
Lues	1
Kernicterus	1
Diabetes mellitus	1
Hypoparathyroidism	1
Pituitary cyst	1
Pituitary adenoma	2
Acoustic neuroma	2
Glioma	7
Metastatic disease	3
Angioma	1
Subarachnoid hemorrhage	1
Subdural abscess	1
Cerebrovascular disease	20
Concussion	3
Undiagnosed	52
No record available	2
Total	500

TABLE III

FINAL CLINICAL DIAGNOSIS IN 500 PATIENTS WITH RADIOLOGIC DIAGNOSIS OF ATROPHY.* GROUP B

Headaches	1
Migraine	3
Optic atrophy	2
Retrobulbar neuritis	1
Labyrinthitis	2
Psychosis	7
Cerebellar and cerebral degeneration	5
Multiple sclerosis	11
Parkinsonism	1
Narcolepsy	1
Epilepsy	28
Mental deficiency	4
Meningitis	2
Encephalitis	3
Neurosyphilis	2
Glioma	1
Angioma	1
Cerebrovascular disease	10
Undiagnosed	22
Peripheral neuritis	1
Amyotrophic lateral sclerosis	1
Cerebrovascular accident	17
Amaurotic familial idiocy	1
Huntington's chorea	1
Brain atrophy	372

The 372 patients with a final clinical diagnosis of brain atrophy were listed as follows:

Postoperative	1
Postirradiation	3
Posttraumatic	10
Postencephalitis	3
Alzheimer's disease	40
Jakob-Creutzfeldt's disease	2
Pick's disease	6
Mental deficiency	13
Psychosis	6
Cerebrovascular disease	80
Cerebrovascular accident	15
Cerebral palsy	9
Multiple sclerosis	9
Parkinsonism	4
Huntington's chorea	6
Epilepsy	27
Chronic alcoholism	3
Neurosyphilis	4
Glioma	2
Little's disease	1
Greenfield's disease	1
Perry-Romberg syndrome	1
Wernicke's encephalopathy	1
Diffuse sudanophilic cerebral sclerosis	1
Lipoidosis	3
Unilateral exophthalmos	1
Brain atrophy, unspecified	120
Total	500

* Dementia was diagnosed in 258 of the 372 patients with, and in 27 of the 128 patients without, brain atrophy. The total number of patients with dementia in Group B was 285.

and dilated ventricular systems.

The radiologic measurement is of importance in investigative and comparative work. The value most frequently quoted[1,7,8] for the maximum width of the ventricular bodies was obtained by Davidoff and Dyke[3] in a study of 150 cerebral air studies. Using a target film distance of 30 inches (76 cm.), they considered as normal a range from 35 mm. to 45 mm. with an average of 40 mm. This compares well with the corresponding value for the upper limit of normal in our series which included 45 mm. for two standard deviations, or 95 per cent of cases. In our material, however, 123 cases, or 25 per cent, had a VS of less than 35 mm. The value for two standard deviations, or 95 per cent of cases, was 29 mm. for the lower limit of normal and the average span measured 37.5 mm. Larsby and Lindgren,[5] in their encephalographic study of epileptic

TABLE IV

FINAL CLINICAL DIAGNOSIS OF 17 PATIENTS OF GROUP A WITH A VENTRICULAR SPAN OF MORE THAN 45 MM.

Clinical Diagnosis	Ventricular Span (mm.)
Epilepsy	46
Mental deficiency	46
Parkinsonism	46
Dementia and brain atrophy	46
Epilepsy	46
Dementia	46
Psychosis	47
Epilepsy	48
Undiagnosed	48
Headache	48
Undiagnosed	48
Headache	48
Dementia	48
Cerebrovascular disease	48
Multiple sclerosis	49
Epilepsy	49
Dementia and brain atrophy	49

Table V

THIRTY-TWO PATIENTS OF GROUP B WITH VENTRICULAR SPAN LESS THAN 45 MM.

Ventricular Span	Dementia	Clinical Atrophy	Diagnosis of	Rounding of Lateral Ventricular Angle
40	Yes	Yes	Postencephalitis	Yes
42	Yes	Yes	Little's disease	Yes
42	Yes	Yes	Alzheimer's disease	Yes
42	Yes	Yes	Cerebrovascular disease	Yes
43	Yes	Yes	Not specified	Yes
43	Yes	No	Cerebrovascular disease	Yes
43	Yes	Yes	Not specified	Yes
43	Yes	Yes	Cerebrovascular disease	Yes
43	Yes	Yes	Primary amentia	Yes
43	Yes	Yes	Pick's disease	Yes
43	Yes	Yes	Mental deficiency	Yes
43	No	No	Cerebrovascular disease	Yes
43	Yes	Yes	Cerebrovascular disease	Yes
44	Yes	Yes	Not specified	Yes
44	Yes	Yes	Greenfield's disease	No
44	Yes	Yes	Jakob-Creutzfeldt's disease	No
44	No	Yes	Not specified	Yes
44	No	Yes	Cerebrovascular disease	No
44	Yes	Yes	Epilepsy	Yes
44	Yes	Yes	Postencephalitic	Yes
44	No	No	Epilepsy	No
44	Yes	No	Encephalitis	Yes
44	Yes	Yes	Not specified	Yes
44	Yes	Yes	Psychosis	Yes
44	Yes	Yes	Not specified	No
44	Yes	Yes	Pick's disease	Yes
44	No	Yes	Not specified	Yes
44	Yes	Yes	Alzheimer's disease	Yes
44	No	No	Cerebrovascular disease	Yes
44	Yes	Yes	Perry-Romberg syndrome	Yes
44	Yes	Yes	Psychosis	Yes
44	Yes	Yes	Mental deficiency	Yes

patients in 1940, considered 46 mm. to 50 mm. as the intermediate range between the normal and the pathologic. Their target film distance was 61 cm. (24 inches). The longer target film distance of modern apparatus produces lower figures. In 234 of our patients (47 per cent) who were considered to have dilated ventricles, the span measured less than 50 mm.

The VS is a practical measurement. It avoids the oblique lines and ratios required by other methods. The reference points at the outer limits of the ventricular bodies at the lateral angle are usually well defined in the brow-up view. Measuring the minimum thickness of the body at the floor of the lateral ventricle, as suggested by Bull,[2] we found less practical. He noted some relationship between this linear measurement and the ventricular volume when re-evaluating the material of Last and Tompsett.[6] Bruijn[1] also thought the size of the lateral ventricular body most closely related to the volume of the ventricular apparatus.

The optimal method for determining the accuracy of the VS measurements is to obtain volumetric data for comparison. Because this was impossible in our material, a comparison of encephalographic figures with the final clinical diagnosis on discharge or subsequent visit was of interest. Such a diagnosis would, of course, be more reliable if a follow-up had been possible in all patients. Further, it may be assumed that the clinician is prejudiced in his diagnostic evaluation of a patient whose ventricular size he knows from a radiologic air study.

We believe, however, that a comparison of the radiologic and clinical diagnosis is permissible if one evaluates the presence or absence of dementia. Dementia is an objective sign for diagnosing or excluding general brain atrophy. It appears significant, therefore, that in Group A, 21 patients (4.2 per cent) showed dementia with a normal VS, in contrast to 285 demented patients (57 per cent) in Group B with ventricular dilatation (Table VII).

Bruijn, conversely to our method, first selected a group of patients with the clinical diagnosis of atrophy and then reviewed their roentgenograms. The fact that the results are comparable in both instances strengthens the argument in favor of the ventricular span measurement.

Not all in Bruijn's group seem to have

Table VI

THIRTY PATIENTS OF GROUP B WITH PROVED DIAGNOSIS

Case	Ventricular Span (mm.)	Dementia	Surgical Inspection of Brain Surface	Biopsy Diagnosis	Necropsy Diagnosis
WB	66	Yes	Atrophy	Inconclusive	
FC	59	Yes	Atrophy	Atrophy	
LR	62	Yes	Atrophy	Normal	
MT	44	Yes	Atrophy	Atrophy	
CB	47	Yes	Atrophy	Normal	
HC	47	Yes	Not stated	Atrophy	
JM	55	Yes	Atrophy	Normal	
SS	61	Yes	Atrophy	Inconclusive	
GE	60	Yes	Not stated	Normal	
HM	58	Yes	Atrophy	Atrophy	
HG	78	Yes	Atrophy	Chronic meningitis	
EH	53	Yes	Atrophy	Cerebrovascular disease	
SH	47	Yes	Not stated	Cerebrovascular disease	
BJ	55	Yes	Atrophy	Atrophy; lipoidosis	
MB	43	No	Atrophy	Normal	
DL	44	Yes	Normal	Normal	
SG	44	Yes	Atrophy	Atrophy; Greenfield's disease	
EK	59	Yes	Normal	Compatible with atrophy	
DG	47	Yes	Atrophy	Atrophy	
AA	49	Yes	Atrophy	Atrophy	Atrophy
PC	51	Not stated	Atrophy	Atrophy	Atrophy
JS	49	Yes	Atrophy	Atrophy	Atrophy and astrocytoma, Grade III
RD	62	No			Astrocytoma, Grade III
PM	48	Yes			Multiple sclerosis
FG	50	Yes			Atrophy
RSJ	53	Yes			Atrophy and astrocytoma, Grade III
JB	58	Yes			Atrophy; lipoidosis
EI	55	Yes			Atrophy; lipoidosis
CL	47	Yes			Atrophy; Pick's disease
DT	44	Yes			Atrophy

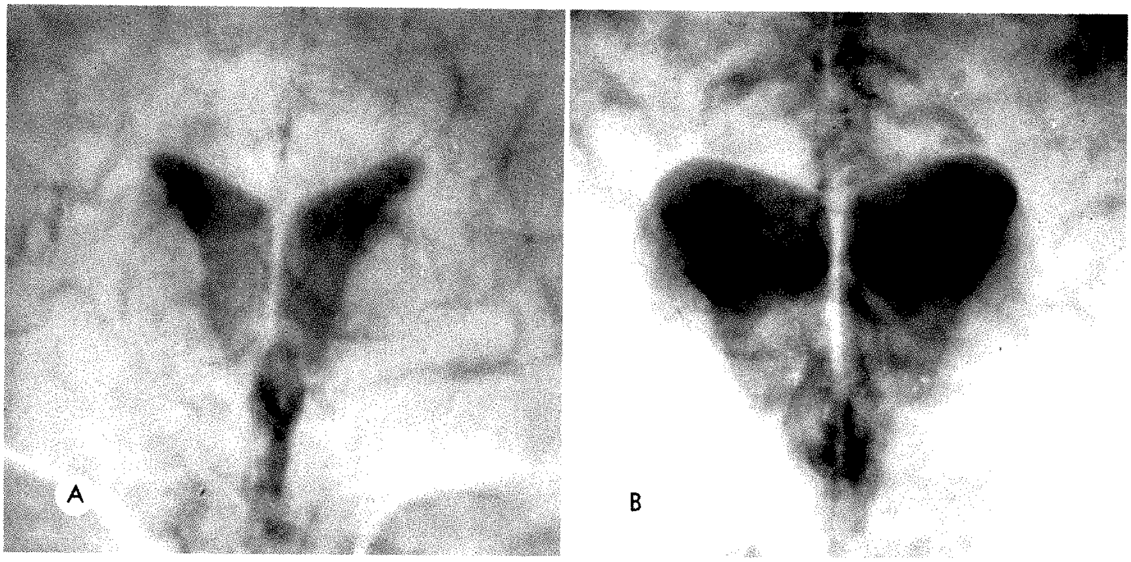


FIG. 5. Replacement of the normally well defined lateral angulation of the ventricular bodies (*A*) by a blunt appearance with pronounced rounding (*B*) is of diagnostic importance in borderline cases.

been patients with general brain atrophy, because some cella media figures were lower than 40 mm.

Knudsen[4] stated, "obtained results of all studies in the literature are inconclusive as regards the normal ventricular size within the different age groups." A pronounced physiologic dilatation of the liquid-containing cerebral chambers with advancing age would certainly render any ventricular measurement in neuroradiology impractical.

We found in our patients of Group A that the VS enlarged only slightly with increasing age (Table I). The increase does not exceed a difference of 2.6 mm. for the first seven decades. This physiologic enlargement represents a variation of only 7 per cent of the over-all average of 37.5 mm. for Group A.

In postmortem studies of 183 adult brains, Knudsen found a more pronounced ventricular-volume increase between the ages of 50 and 60 years, which is similar to our results. In the 70 to 80 year age group, he showed further enlargement. Unfortunately, not enough patients more than 70 years of age were available for study in our own Group A. A representative number of cases, however, is presented in the age groups between 10 and 60 years. The mean VS in the presumably normal patient is shown to increase from the second to the sixth decade of life by not more than 0.6 mm., a remarkably small relative change with increasing age.

SUMMARY AND CONCLUSION

In a review of 500 cerebral air studies interpreted as normal by the neuroradiologist, the VS measurement for two standard deviations, or 95 per cent of patients,

TABLE VII

VENTRICULAR SPAN AND CLINICAL DIAGNOSIS

	Ventricular Span	
	Normal (Group A)	Enlarged (Group B)
No. of patients with dementia	21	285
No. of patients with atrophy	14	372
No. of patients with cerebrovascular disease	20	122

showed a range from 29 mm. to 45 mm. (Group A).

Of another 500 patients, but with ventricular systems considered radiologically to be dilated, and a diagnosis of brain atrophy, 93.5 per cent had a ventricular span of 45 mm. or more (Group B).

The average VS in Group A was 37.5 mm.

An increase of no more than 1.5 mm. (4 per cent) was found for the mean physiologic dilatation in patients ranging from the second to the seventh decade of life.

Twenty-one patients of Group A and 285 patients of Group B were demented.

In the group of cases with dilatation, dementia appeared as a frequent clinical sign of atrophy, whereas brain biopsy was dependable only when positive.

The range of normal and the average normal width of the ventricular bodies are less than previously described, but the effect of target film distance must be taken into account.

A given patient with a VS larger than 45 mm. has a 2.5 per cent chance of being normal. A given patient with a VS smaller than 45 mm. has a 6.5 per cent chance of having generalized brain atrophy. Rounding of the lateral ventricular angles is of diagnostic importance in borderline cases.

Asymmetry of the lateral ventricles would seem to occur in about 30 per cent of normal cases with a preponderance in the left at a ratio of 2.5:1.

The VS measurement shows a relation to ventricular volume.

The VS is a practical radiographic measurement in cerebral pneumoencephalography.

H. Joachim Burhenne, M.D.
Department of Radiology
University of California
San Francisco Medical Center
San Francisco 22, California

The authors wish to thank the Medical Committee and the Physicians and Surgeons of the National Hospital, Queen Square, London, for permission to use the case records of the patients studied.

REFERENCES

1. Bruijn, G. W. Pneumoencephalography in diagnosis of cerebral atrophy: quantitative study. Thesis. State University of Utrecht, 1959.
2. Bull, J. W. Volume of cerebral ventricles. *Neurology*, 1961, *11*, 1–9.
3. Davidoff, L. M., and Dyke, C. G. The Normal Encephalogram. Second edition. Lea & Febiger, Philadelphia, 1946, p. 96.
4. Knudsen, P. A. Ventriklernes størrelsesforhold i anatomisk normale hjerner fra voksne mennesker. Thesis, Copenhagen. Andelsbogtrykkeriet, Odense, 1958.
5. Larsby, H., and Lindgren, E. Encepahlographic examinations of 125 institutional epileptics. *Acta psychiat. et neurol.*, 1940, *15*, 337–352.
6. Last, R. J., and Tompsett, D. H. Casts of cerebral ventricles. *Brit. J. Surg.*, 1953, *40*, 525–543.
7. Lusted, L. B., and Keats, T. E. Atlas of Roentgenographic Measurement. Year Book Publishers, Inc., Chicago, 1959.
8. Orley, A. Neuroradiology. Charles C Thomas, Publisher, Springfield, Ill., 1949, p. 207.

◆

TUBERCULOMA OF THE BRAIN*

By LEONARD BERLIN, M.D.
CHICAGO, ILLINOIS

AN OLD adage in medicine is that if one does not think of the correct diagnosis, he will never arrive at it. In the case of tuberculoma of the brain, this tenet is especially appropriate, for this disease entity, although relatively uncommon, occurs with enough frequency to completely surprise and confound unsuspecting clinicians and radiologists at the time of surgery or autopsy on at least several occasions. It is the purpose of this report to provide the radiologist with a conception of intracranial tuberculoma that will enable him to make an early presumptive diagnosis when confronted with certain clinical and roentgenologic findings. Because of recent advances in therapy and dramatic improvement in survival rates, a high level of suspicion on the part of the radiologist for this disease can be lifesaving for the patient.

PATHOPHYSIOLOGY

The tubercle bacillus usually enters the body through the lungs, although other ports such as the tonsils, intestines, or lymph nodes are occasionally used.[26] The tissues respond to this invasion by formation of the classic tubercle: a combination of large mononuclear epithelioid cells, multinucleated Langhans' giant cells, and a peripheral zone of lymphocytes. At this point the local lesion may disseminate tubercle bacilli to distant areas by various routes, the most frequent being hematogenous.[21] In this manner miliary tubercles may form in the brain and meninges.

Depending on many factors, among which are the number and virulence of the bacilli and the resistance of the host, the tubercles in the brain can take several courses. They may completely regress; they may progress and cause tuberculous meningitis; or they may form a tuberculous granuloma or tuberculoma.[12] A tuberculoma, then, is a mass of granulation tissue consisting of a central core of caseation necrosis surrounded by a zone of giant and inflammatory cells, all encased in a well-developed capsule.[27] Grossly, these are hard, well-circumscribed avascular masses, measuring from several millimeters to 3–4 cm. in diameter.[10] Figure 1 shows this typical appearance. The largest one reported occupied an entire half of one hemisphere.[26] Because the bacilli found in the brain are blood borne and because of the rather abundant blood supply to the cortex of the cerebrum and cerebellum, tuberculomas tend to be situated in these areas.[13,20] In patients under 20 years of age, the lesions are usually found beneath the cerebellar tentorium; after the age of 20, supra- and infratentorial tuberculomas are noted about equally,[1] with perhaps the supratentorial lesions being slightly more frequent.[19]

Solitary tuberculomas greatly outnumber multiple ones, about 4 to 1.[9,16] Once formed, the tuberculoma behaves like a space-occupying lesion. Before the days of antibiotics, most cases ended fatally with tuberculous meningitis;[29] occasionally, the progression of a tuberculoma is halted spontaneously and calcification of the lesion occurs.[27]

In summary, then, it must be emphasized that the intracranial tuberculoma is always secondary to a tuberculous infection elsewhere in the body,[24] although the primary focus may not be active or clinically evident.[6] Lewison *et al.*[16] reviewed 757 consecutive autopsies of patients afflicted with tuberculosis and found that 20, or just under 3 per cent, had brain tuberculomas.

INCIDENCE

Tuberculomas were first reported in the literature by Ford[29] in 1790 and appeared to be quite prevalent in the late nineteenth

---

* From the Department of Radiology, College of Medicine, University of Illinois, Chicago, Illinois.

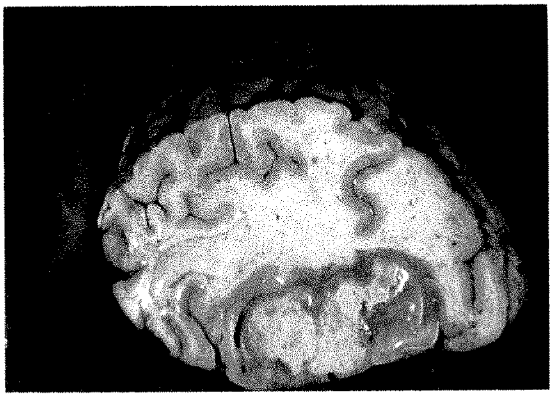


Fig. 1. Coronal section of left occipital lobe of the brain in Case 8, showing the well-encapsulated, round 2×4 cm. lesion. This is the typical gross appearance of tuberculoma of the brain.

century. The incidence of tuberculomas among brain tumors was reported as high as 50 per cent in 1890, but the validity of these reports is somewhat questionable.[17,30] A more generally accepted figure is that given by Van Wagenen[30] in 1927, who reviewed Harvey Cushing's 1,000 cases of proven brain tumors at the Peter Bent Brigham Hospital and arrived at an incidence of 1.4 per cent. Other American authors report similar figures, namely between 1 and 3 per cent.[6,13,20,32] Reports from England,[12,14] Romania,[1] and Germany[35] show statistics within the same range. However, the incidence in many other countries is considerably higher, and from these we gain much of our knowledge of tuberculomas. These lesions account for 20 per cent of the brain tumors in Chile,[4] 20 per cent in India,[10,25] 8 per cent in Panama,[15] 4 per cent in Spain,[22] and similarly high statistics are reported from southern Europe, southern Russia, South America and Asia.[26]

Scott and Graves[29] reviewed 815 cases of tuberculomas of the brain up to the year 1933 and noted that 49 per cent occurred before the age of 10 years. Practically all authors state that most of the cases occur before the age of 30.[7,11,14,15,16] The youngest age reported is 23 days;[35] the oldest, 68 years.[1] Scott and Graves also found that males outnumbered females 2 to 1. Unquestionably, the incidence in recent years has been steadily decreasing due to the use of both BCG vaccine[2] and antituberculous drugs.[5,22]

MATERIAL AND RESULTS

A review of the records of the University of Illinois Research and Educational Hospitals in the 27 year period from 1935 until the present disclosed 10 proven cases of tuberculoma of the brain. Only cases proven by autopsy or surgery were gathered for this study; presumptive cases based on clinical, roentgenologic or laboratory findings without histologic proof were not used. In Table I these cases with the clinical and laboratory findings, treatment, and course of each are listed.

As can be seen, the ages ranged from 6 to 60 years, with 6 of the cases being between the ages of 15 and 24. It should be pointed out that known tuberculous patients as a rule are not admitted to our hospital; this undoubtedly is the reason for the low number of tuberculomas which were seen. Despite this, 8 of our 10 patients had active tuberculosis demonstrated elsewhere in the body, 6 of which were afflicted with systemic disease. All of our cases were rather far advanced, most dying within days or weeks after admission.

Symptoms usually included manifestations of increased intracranial pressure, namely, visual difficulties and headaches. Convulsions and specific localized neurologic deficits were common. Roentgenograms demonstrated signs of increased intracranial pressure (Fig. 2 *A*). Ventriculograms usually showed the location of a space-occupying lesion (Fig. 3, *A* and *B*; and 4, *A* and *B*). Cerebral arteriography was performed only once (Case 7), but was noncontributory, since only the anterior and middle cerebral arteries were visualized in a patient who had a posterior fossa lesion.

DISCUSSION

These 10 cases illustrate certain important characteristics of this disease entity, helpful to both the clinician and the radiologist. A review of these is in order.

TABLE I

Patient and Year of Admission	Age (yr.)	Race	Sex	Duration of Illness	Symptoms	Physical Examination	Previous History	Spinal Tap	Roentgenographic Findings	Surgery and Course	Autopsy Findings
1. E.S. 1936	60	W	Male	6 mo.	Right hemiparesis; double vision; personality changes	Papilledema; aphasia	Negative	—	No record	Craniotomy showed flat convolutions, no tumor; died 5 wk. later	3 tuberculomas in basal ganglia and both frontal lobes
2. R.P. 1937	22	W	Male	2 wk.	Occipital headaches	Papilledema; 6th nerve palsy	Pneumonia in childhood	Increased pressure; increased protein	Dilatation of lateral and 3rd ventricles	Surgery showed left cerebellar tumor; died 5 mo. later	1.5 cm. left cerebellar tuberculoma and tuberculous meningitis
3. L.B. 1938	15	N	Male	2 yr.	Loss of vision; occipital headaches; personality changes; left hemiparesis; staggering gait	Optic nerve atrophy	Negative	—	Calcification of right parietal area	Died just prior to surgery	Orange size tuberculoma of right parietal lobe and tuberculosis of lung, liver and spleen
4. T.M. 1943	24	N	Male	7 mo.	Convulsion; headaches; hemiparesis; double vision	Papilledema	Pulmonary tuberculosis until 2 mo. previously	—	Diastasis of sutures	Died at time of ventriculography	3 cm. left cerebellar and 1.5 cm. right frontal tuberculoma; tuberculous meningitis; systemic active tuberculosis
5. R.T. 1944	18	N	Female	3 mo.	Convulsions; headache; diplopia	Incontinence; stupor; 6th nerve palsy; left hemiparesis	Pulmonary tuberculosis until 6 mo. previously	Increased pressure; positive culture for tuberculosis	Normal plain roentgenograms	Decompression only; died 1 mo. later	Multiple tuberculomas of frontal lobes; tuberculous meningitis; tuberculosis of lung
6. A.H. 1945	17	N	Female	10 mo.	Headache; impaired vision	Papilledema; rigid neck; blindness; absent light reflex	Negative; 5 mo. pregnant	Increased pressure; positive serology	Dilatation of lateral and 3rd ventricles	Surgery showed inoperable cerebellar tumor; died 6 wk. later	6 cm. tuberculoma of left cerebellar hemisphere; tuberculosis of lung
7. C.D. 1952	22	N	Male	2 mo.	Headache; diplopia; numbness of right hand; unsteady gait	Papilledema; right hemiparesis; 6th nerve plasy	Pneumonia 5 yr. previously	Normal	Angiography negative; dilatation of lateral and 3rd ventricles	Exploratory negative; died 3 da. later	Tuberculoma involving 2/3 of pons; tuberculosis of lung and adrenal
8. A.D. 1953	40	N	Female	2 wk.	Headache; fever	Exophthalmos; rigid neck; comatose	10 yr. history of multiple abdominal draining sinuses with many surgical procedures	Increased pressure; positive Pandy test	Dilatation of lateral and 3rd ventricles	Died after ventriculography; no surgery	2×4 cm. tuberculoma of left occipital lobe; tuberculous meningitis; systemic tuberculosis including mesentery
9. S.T. 1953	6	W	Female	1 yr.	Abdominal pain; vomiting; chronic fever; weight loss, lethargy	Emaciation; acutely ill; right chronic otitis; papilledema	Negative	—	Increased convolutional markings	Frontal decompression; died several hours later	Multiple tuberculomas of corpora quadrigemina and frontal lobes; tuberculous meningitis; tuberculosis of lungs, liver, mesentery and right middle ear
10. C.W. 1954	39	N	Female	1 yr.	Epilepsy; headaches	Papilledema; positive Hoffmann sign	Pulmonary tuberculosis 3 yr. previously	—	Erosion of posterior clinoids; displacement of lateral ventricles to left	Parietal decompression; died 4 hr. after surgery	Large tuberculoma of right parietal area; tuberculosis of lungs, liver and spleen

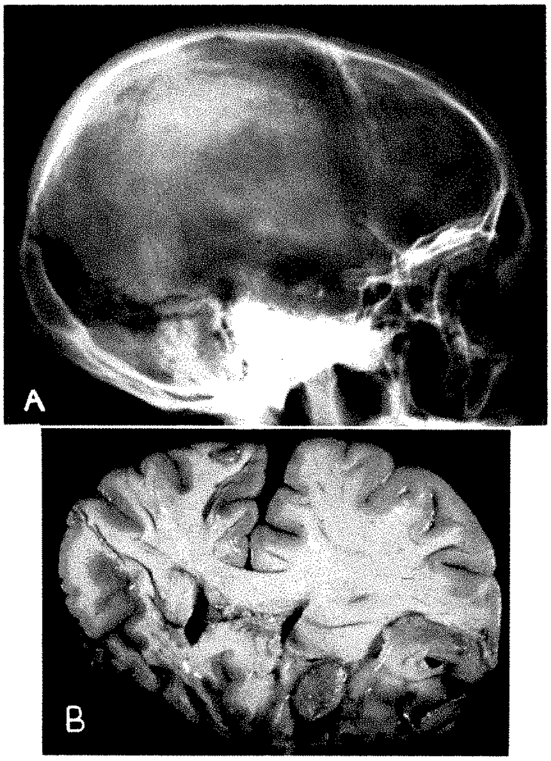


Fig. 2. Case 4. (*A*) Plain roentgenogram showing diastasis of sutures and erosion of posterior clinoids and dorsum sellae, suggestive of a space-occupying lesion. (*B*) Coronal section of frontal lobes showing the 1.5 cm. diameter tuberculoma on the right. The accompanying cerebellar lesion is not visualized.

The plain skull roentgenogram of Case 3 (Fig. 5, *A* and *B*) demonstrated a round calcification, 3 cm. in diameter, in the right parietal area corresponding to the tuberculoma. Calcification of a brain tuberculoma is a somewhat unusual phenomenon. Most authors agree that the occurrence is rare, a strange fact since pulmonary tuberculomas calcify quite frequently. From Romania a calcification incidence of 5 per cent was reported,[1] in Chile, calcification was noted to occur in 1 out of 96 cases,[9] and in the United States a rate of 8 per cent was recorded.[13] However, these statistics may be too high, since many included unproven cases. In 1952, Lorber[17] made a thorough search of the literature to date and found 49 cases of reported calcifications in brain tuberculomas. Thirteen of these were postmortem findings; the calcifications were not visualized on roentgenograms. Of the remaining 36 which did demonstrate calcifications on plain roentgenograms of the skull, only 14 were histologically proven; 22 were presumptive diagnoses which had neither biopsy nor autopsy substantiation.

Scott and Graves in the earlier review of 815 cases of tuberculoma mentioned only 11 cases of calcification. In 1961 Ramamurthi

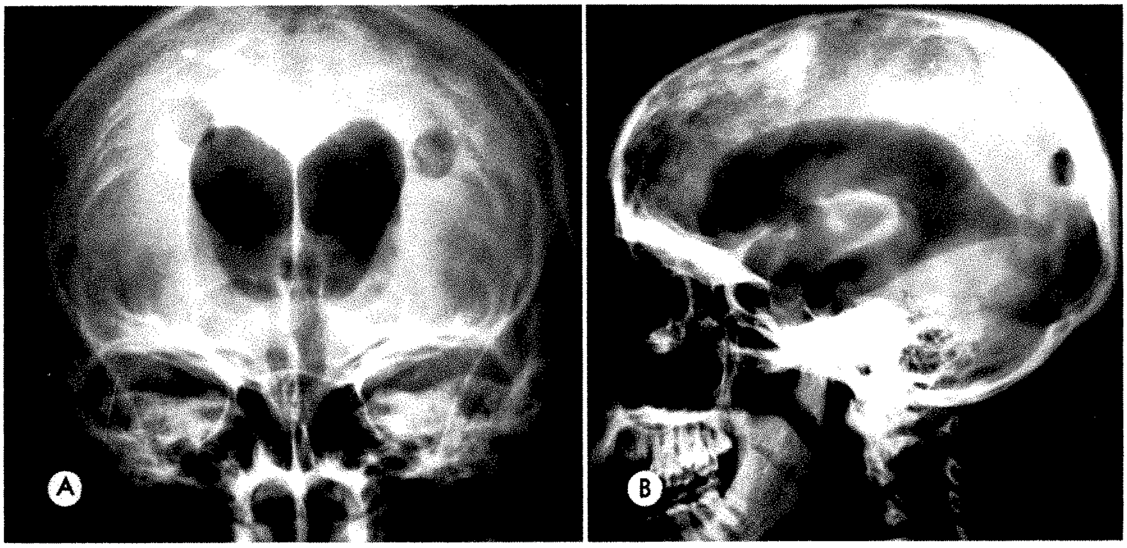


Fig. 3. Case 6. Posteroanterior (*A*) and lateral (*B*) ventriculograms showing abnormal dilatation of both lateral and third ventricles, with apparent obstruction of the aqueduct of Sylvius. Autopsy disclosed a 6 cm. in diameter cerebellar tuberculoma.

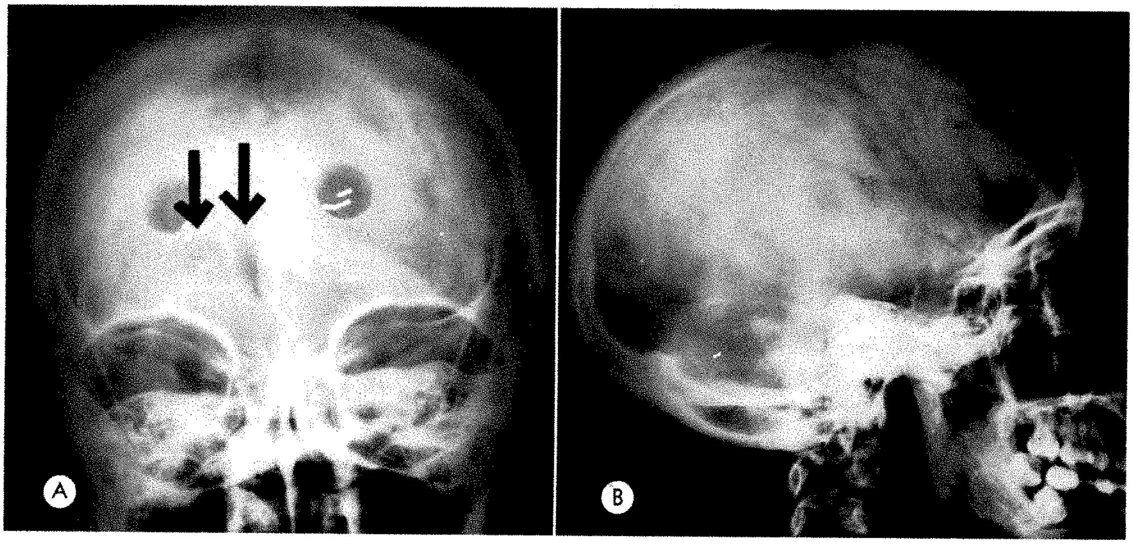


FIG. 4. Case 10. (*A* and *B*) In these roentgenograms note the erosion of the posterior clinoids and the displacement of normal sized lateral ventricles to the left (*A* is reversed). Autopsy revealed a large tuberculoma of the right parietal area.

et al.[26] reporting 175 cases of tuberculoma, found calcifications in but 6 roentgenographically; however, they state that microscopic calcification is much more frequently noted. Perhaps one of the reasons that so few calcified lesions are seen is because not all tuberculous patients have skull roentgenograms.[34] Evans and Courville[15] believe that the incidence is low since tuberculoma patients usually die of meningitis before a significant deposition of calcium can occur. In support of this theory, Lorber[17] followed 25 children who had been treated and cured of tuberculous meningitis, and found that all of them developed calcifications which were visible on skull roentgenograms within 18 months to 3 years. Although the exact location of these deposits was not determined, he felt they lay in regions of an inactive tuberculoma, an old encephalitis, encephalomalacea resulting from an infarct, or a scarred exudate in the meninges.

Calcification represents healing of the tuberculoma, but it is not an indication of continued quiescence.[13] The calcific deposits usually occur at the junction of the necrotic caseous center and the surrounding hyalinized connective tissue. The calcareous layer therefore usually assumes a ring shape initially. As the outer zone of connective tissue shrinks and as the necrotic center is absorbed or calcifies, this initial calcareous ring is fractured. Therefore, an irregular broken calcareous shell is characteristic of a tuberculoma—it does not occur in any other intracranial tumor.[8,18,23] Figure 5, *A* and *B* is an example of this appearance. In their monograph on intracranial calcifications, Mascherpa and Valentino[19] label such calcification as the "lobulated" type. They point out that a large, 1–3 cm. in diameter calcification which is dense and jagged at the periphery and radiolucent in the center can also resemble a spongioblastoma. They also describe a less common and more nonspecific pattern of tubercular calcifications, which they call the "nodular" type. This is composed of multiple calcareous concretions, grouped together. These must be differentiated from craniopharyngioma, angiomas, subdural hematoma, ependymoma, tuberous sclerosis, and toxoplasmosis.[33]

DIAGNOSIS

Tuberculoma of the brain can be suspected preoperatively only by correlating the clinical picture with the roentgenographic and laboratory findings. By these means Arseni[1] was able to make a correct

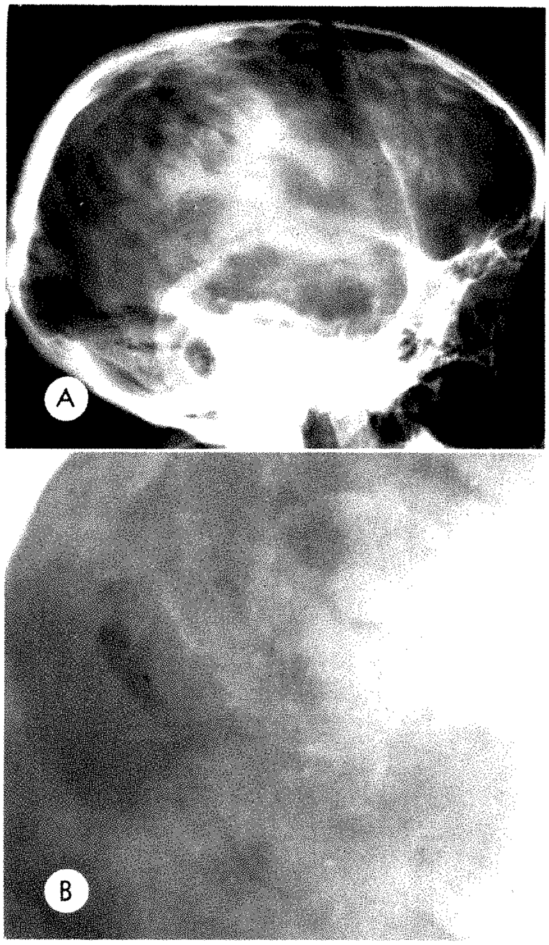


Fig. 5. Case 3. (*A*) Lateral skull roentgenogram showing a large, faintly calcified lesion in the parietal area. (*B*) Enlarged close-up view of this lesion showing the fractured shell appearance of the calcified portion, characteristic of tuberculoma of the brain.

preoperative diagnosis in 85 per cent of 201 cases.

The patient's history is most important. Approximately one-third to one-half of the patients give a history of either previous active tuberculosis elsewhere in the body or of contact with tuberculosis.[21,25] In another 30 to 50 per cent, a search of the lymphatic system, the lungs and pleura, the bones, and the urinary and genital tracts will uncover evidence of concomitant active tuberculosis in one or more of these areas.[2,22] The patient's environment is also important; poor living conditions and/or debilitating diseases are common in tuberculosis.

Symptoms are those of any expanding lesion of the brain. If the tuberculoma is supratentorial, there are symptoms and signs of increased intracranial pressure: headaches, vomiting, loss of vision, etc. If infratentorial, in addition to the above findings there are cerebellar disorders, such as ataxia, nystagmus, etc.[16,22] Physical examination is equally nonspecific as to etiology. Nearly all patients show papilledema;[10] some cases may be entirely asymptomatic.[33]

Laboratory studies include skin tests, and blood and spinal fluid work-up. Electroencephalography has recently been shown to be of value in the diagnosis of this disease.[31]

Roentgenographic studies are helpful. Plain roentgenograms of the skull show the well-known signs of increased intracranial pressure: diastasis of the sutures, increased convolutional markings, erosion of the dorsum sellae, etc.[9] Rarely, the "characteristic" calcification described above may be visualized. Ventriculographic studies usually will localize a space-occupying lesion.[15]

The use of cerebral angiography in the diagnosis of this entity has been well described by Ramamurthi and Varadarajan,[25] who perform this examination in almost every suspected supratentorial lesion. They describe two types of angiographic lesions: first, the avascular tuberculoma which is deep-seated, acts like a space-occupyiny mass clinically, and which is treated by surgery (this is by far the most frequent); second, the vascular tuberculoma which is superficial in location and not benefited bg surgery. The latter is exceedingly rare. These authors feel that angiography is quite helpful not only because they frequently diagnose and localize the tuberculoma by this means, but also because the method will occasionally reveal the presence of a glioma or other tumor instead of the clinically suspected tuberculoma. The authors describe other characteristic angiographic findings, for which the reader is referred to their excellent report.

Obrador[22] emphasizes the importance of early diagnosis. It is urgent that treatment be instituted before permanent damage from increased intracranial pressure, usually blindness, occurs.

TREATMENT AND PROGNOSIS

Prior to the antibiotic era, treating brain tuberculomas was difficult. Harvey Cushing is said to have advised only surgical decompression, since neither surgery nor any other treatment would effect a cure. Mortality rates were reported as high as 80 per cent.[1] With the advent of streptomycin, isoniazid and other antituberculous medical drugs, the picture has changed dramatically. The combination of drug and surgical therapy has become the treatment of choice and has been able to lower the mortality rates to 10–15 per cent.[15,26]

Recently, several authors have suggested that medical therapy alone will give as good if not better results than the combined surgery-drug approach. Roedenbeck[28] treated 32 children with drugs only; 26 survived and 13 are completely well. He feels that drugs eliminate surgery as the treatment of choice and that medication is the only effective means of treatment. Other authors are less enthusiastic. They feel that medical therapy should be instituted in all suspected cases of brain tuberculoma, but that surgery should be performed if the patient does not improve rapidly.[2,3]

SUMMARY AND CONCLUSIONS

A review of the literature is presented and 10 cases of tuberculoma of the brain from the University of Illinois Research and Educational Hospitals are reported. The following important points are stressed.

1. In the United States and England, this entity accounts for 1–3 per cent of all brain tumors. The incidence is as high as 20 per cent in countries of South America, Asia, and southern Europe.

2. An early diagnosis of this condition is essential if a cure is to be effected. A preoperative diagnosis can be made in as many as 85 per cent of the patients by correlating the history, clinical and laboratory findings, and roentgenographic studies. Above all, a high level of suspicion on the part of the clinician and radiologist is most essential in the diagnosis. One must think of tuberculoma in order to diagnose it.

3. Calcification of tuberculomas is rare, occurring in less than 5 per cent of the cases. A not too common finding on the plain roentgenogram of the skull, that of a fractured calcareous shell, is characteristic of this entity.

4. Current treatment, consisting primarily of antituberculous drugs suplemented by surgery when necessary, can produce cures in as many as 90 per cent of the patients. It therefore behooves the diagnostician to be aware of this condition.

840 South Wood Street
Chicago 12, Illinois

ADDENDUM

Subsequent to the writing of this report, an eleventh case of tuberculoma of the brain has been seen at our hospital. The patient, A.J., a 31 year old Negro male, presented with a 10 month history of occipital headaches and dizzy spells. Physical findings included papilledema and right facial nerve weakness. No history of tuberculosis was present, but chest roentgenograms revealed diffuse bilateral infiltrations. Sputum culture was positive for tubercle bacilli. A ventriculogram showed dilated lateral ventricles with a shift of the aqueduct of Sylvius to the right; a brachial arteriogram showed questionable anterior displacement of the basilar artery. The patient was placed on isoniazid, PAS and streptomycin. Ten days later a craniotomy was performed, revealing a large left cerebellar tuberculoma. The lesion was removed completely and the patient had an unremarkable postoperative course. His symptoms improved markedly, but the patient developed a psychosis, possibly related to the administration of the antituberculous drug isoniazid. He was transferred to a tuberculosis sanitarium for convalescence, but shortly thereafter committed suicide by leaping from an open window.

REFERENCES

1. Arseni, C. Two hundred and one cases of intracranial tuberculoma treated surgically. *J. Neurol., Neurosurg. & Psychiat.*, 1958, *21*, 308–311.
2. Asenjo, A. Tuberculomas of brain: general remarks. *Neurocirugía*, 1961, *19*, 311–312.
3. Asenjo, A., Fierro, J., and Carrizo, F. Tratamiento de los tuberculomas cerebrales. *Neurocirugía*, 1961, *19*, 394–407.
4. Asenjo, A., Valladares, H., and Fierro, J. Tuberculomas of brain: report of 159 cases. *A.M.A. Arch. Neurol. & Psychiat.*, 1951, *65*, 146–160.
5. Bagchi, A. Intracranial tuberculomas. *J. Indian M. A.*, 1961, *37*, 429–433.
6. Bernstein, T. C., Krueger, E. G., and Nayer, H. R. Tuberculoma of brain; surgical removal in presence of widespread tuberculosis. *Am. Rev. Tuberc.*, 1950, *62*, 654–666.
7. Buchstein, H. F., and Adson, A. W. Tuberculoma of brain. *A.M.A. Arch. Neurol. & Psychiat.*, 1940, *43*, 635–648.
8. Camp, J. D. Pathologic non-neoplastic intracranial calcification. *J.A.M.A.*, 1948, *137*, 1023–1031.
9. Castro, M., and Lepe, A. Radiología del tuberculoma cerebral. *Neurocirugía*, 1961, *19*, 377–382.
10. Chandy, J., and Isaiah, P. Tuberculomas of brain. *J. Indian M. A.*, 1952, *21*, 239–242.
11. Descuns, P., Garre, H., and Pheline, C. Tuberculomas of brain and cerebellum. *J. Neurosurg.*, 1954, *11*, 243–250.
12. Dott, N. M., and Levin, E. Intracranial tuberculoma. *Edinburgh M. J.*, 1939, *46*, 36–41.
13. Evans, H. S., and Courville, C. B. Calcification and ossification in tuberculoma of brain. *A.M.A. Arch. Surg.*, 1938, *36*, 637–659.
14. Garland, H. G., and Armitage, G. Intracranial tuberculoma. *J. Path. & Bact.*, 1933, *37*, 461–471.
15. Gonzales-Revilla, A. Intracranial tuberculomas: experience with 10 consectuive cases. *J. Neurosurg.*, 1952, *9*, 555–563.
16. Lewison, M., Freilich, E. B., and Ragins, O. B. Tuberculoma of brain. *Ann. Int. Med.*, 1934, *7*, 1141–1145.
17. Lorber, J. Incidence and nature of intracranial calcifications after tuberculous meningitis. *Arch. Dis. Childhood*, 1952, *27*, 542–551.
18. Martin, J. P. Calcified intracranial tuberculomata. *Brit. J. Radiol.*, 1937, *10*, 5–18.
19. Mascherpa, F., and Valentino, V. Intracranial Calcification. Charles C Thomas, Publisher, Springfield, Ill., 1959, pp. 52–55.
20. Mudd, R., Perlmutter, I., and Strain, R. E. Calcified intracranial tuberculoma with report of case. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1955, *73*, 19–22.
21. Diagnostic Standards and Classification of Tuberculosis. National Tuberculosis Assoc., New York, 1961, p. 50.
22. Obrador, S. Intracranial tuberculomas: review of 47 cases. *Neurochirugía*, 1959, *1*, 150–157.
23. Pendergrass, E. P., Schaeffer, J. P., and Hodes, P. J. The Head and Neck in Roentgen Diagnosis. Second edition. Charles C Thomas, Publisher, Springfield, Ill., 1956, pp. 1043–1048.
24. Ramamurthi, B. Experiences with tuberculomas of brain. *Indian J. Surg.*, 1956, *18*, 452–455.
25. Ramamurthi, B., and Varadarajan, M. G. Diagnosis of tuberculomas of brain: clinical and radiological correlation. *J. Neurosurg.*, 1961, *18*, 1–7.
26. Ramamurthi, B., Varadarajan, M. G., and Verdachlam, S. P. Tuberculoma of brain: pathologic picture and diagnosis. *J. Internat. Coll. Surgeons*, 1961, *35*, 605–611.
27. Robbins, S. L. Textbook of Pathology with Clinical Application. Second edition. W. B. Saunders Company, Philadelphia, 1962, p. 1117.
28. Roedenbeck, S. D. Tuberculomas of nervous system in children: report of 32 cases. *World Neurol.*, 1962, *3*, 55–65.
29. Scott, E., and Graves, G. O. Tuberculoma of brain: with report of four cases. *Am. Rev. Tuberc.*, 1933, *27*, 171–192.
30. Van Wagenen, W. P. Tuberculoma of brain: its incidence among intracranial tumors and its surgical aspects. *A.M.A. Arch. Neurol. & Psychiat.*, 1927, *17*, 57–92.
31. Villavicencio, C., Pena, A., and Chediack, C. El electroencefalograma en los tuberculomas encefalicos. *Neurocirugía*, 1961, 390–393.
32. Walker, A. E., and Hopple, T. L. Brain tumors in children: general considerations. *J. Pediat.*, 1949, *35*, 671–687.
33. Weens, H. S. Calcified intracranial tuberculomas. *J. Pediat.*, 1948, *33*, 328–335.
34. Weinberger, L. M., and Grant, F. C. Calcified tuberculoma of brain. Am. J. Roentgenol. & Rad. Therapy, 1942, *47*, 525–533.
35. Zulch, K. J. Brain Tumors—Their Biology and Pathology. Springer Publishing Co., Inc., New York, 1957, pp. 242–244. American edition translated by Alan B. Rothballer and Jerzy Olszewski.

DIENCEPHALIC PSEUDOTUMOR EFFECT*

By LEON LOVE, M.D.,† SANFORD J. LARSON, M.D.,‡ *and* BEAUVOIR EDMOND, M.D.§
CHICAGO, ILLINOIS

THE normal vascular pattern of the thalamus, hypothalamus, and basal ganglia presents itself as a homogeneous vascular blush, which can be a source of diagnostic error if one is not aware of this finding. Our attention was called to this in a case of occlusion of the middle cerebral artery in which the normal thalamus mimicked the tumor stain of a meningioma. The use of serial roentgenograms enables one to observe this normal appearance with relative ease in many cases. In occlusive disease, particularly of the middle cerebral artery, an unobstructed view of the central structures is obtained.

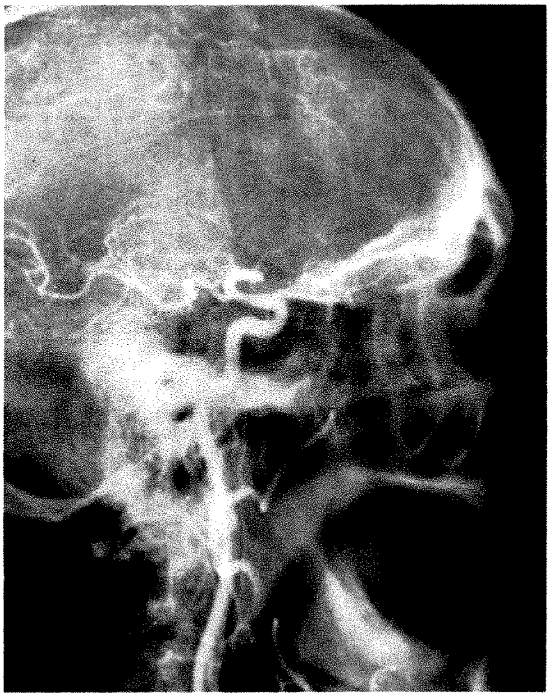


Fig. 1. Case 1. Serial left lateral roentgenogram at 3 seconds. There is faint visualization of the anterior cerebral artery and occlusion of the middle cerebral artery. The posterior communicating artery gives off branches to the thalamus and hypothalamus. Note the beginning vascular blush.

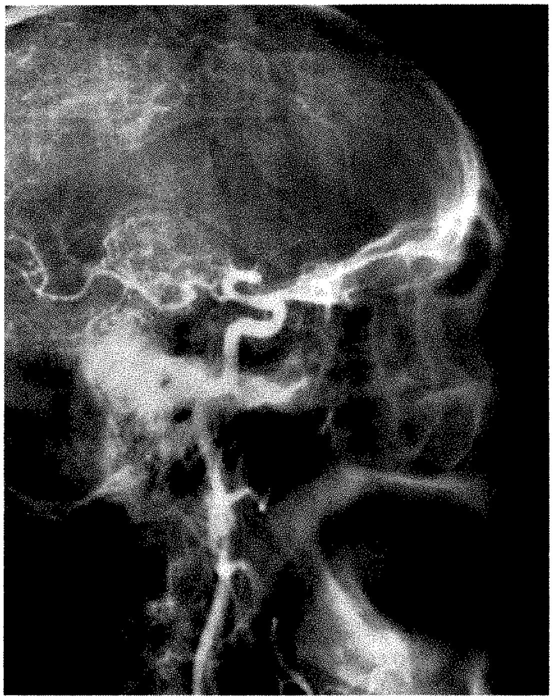


Fig. 2. Case 1. Serial roentgenogram at $4\frac{1}{2}$ seconds. There is slight increase in the vascular blush above the posterior communicating artery.

The hypothalamus, thalamus, and basal ganglia are deeply situated, paired, cerebral structures lying on either side of the third ventricle, and approximately coextensive with it.

The blood supply is as follows: The hypothalamus receives its blood supply from the circle of Willis, particularly the anterior cerebral artery, the anterior communicating artery, and the posterior communicating artery. The central diencephalic arteries course vertically to the

---

* From the Departments of Radiology, Neurosurgery, and Surgery, Cook County Hospital, Chicago, Illinois.

† Director of Diagnostic Radiology, Cook County Hospital; Associate Professor of Radiology, The Chicago Medical School.

‡ Formerly, Director of Neurosurgical Education, Cook County Hospital; presently Director of Neurosurgery, Marquette University, Milwaukee, Wisconsin.

§ Resident in Radiology, Cook County Hospital.

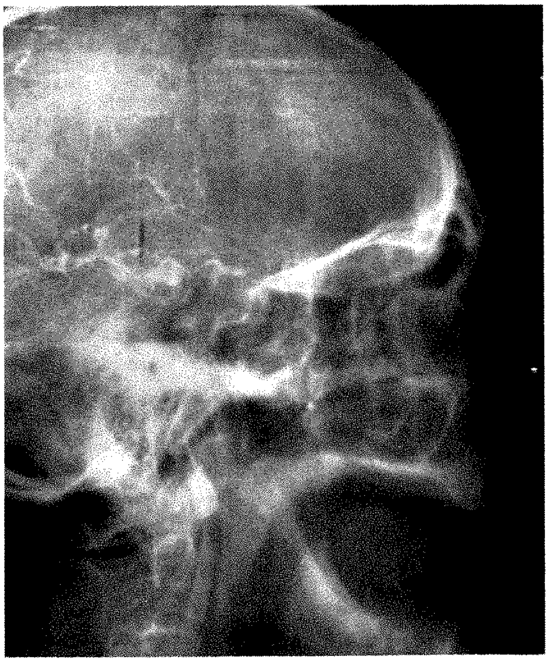


Fig. 3. Case I. Serial roentgenogram at 6 seconds. The vascular blush is more definite.

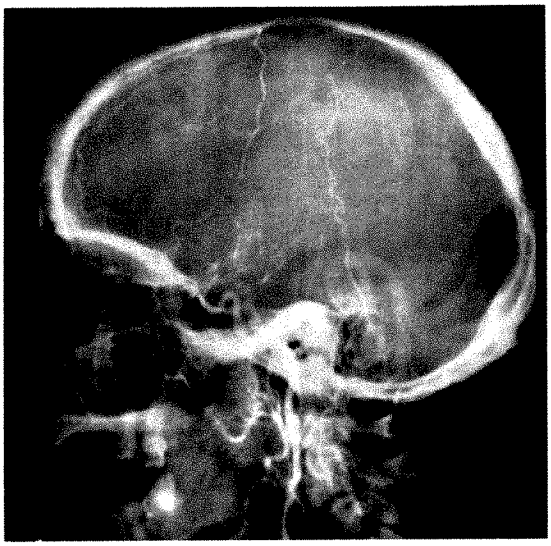


Fig. 5. Case II. Right carotid lateral arteriogram. There is occlusion of the internal carotid artery at its bifurcation. Note the vascular blush immediately above the dorsum sellae.

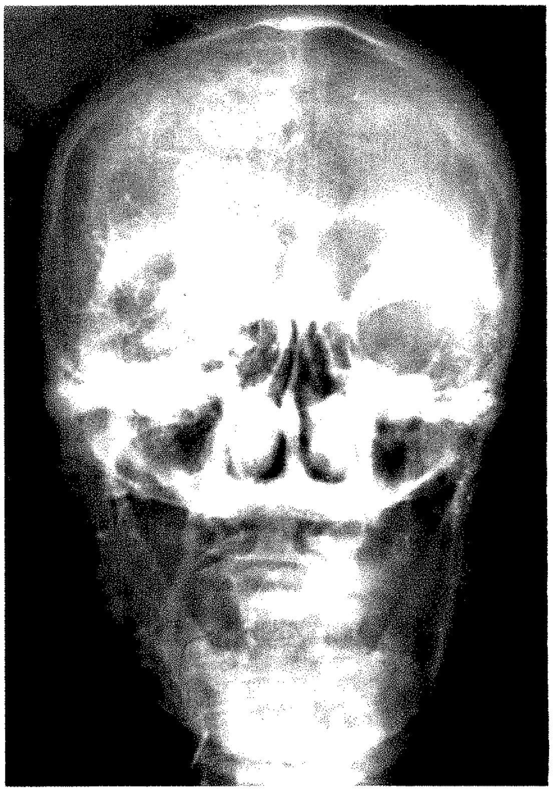
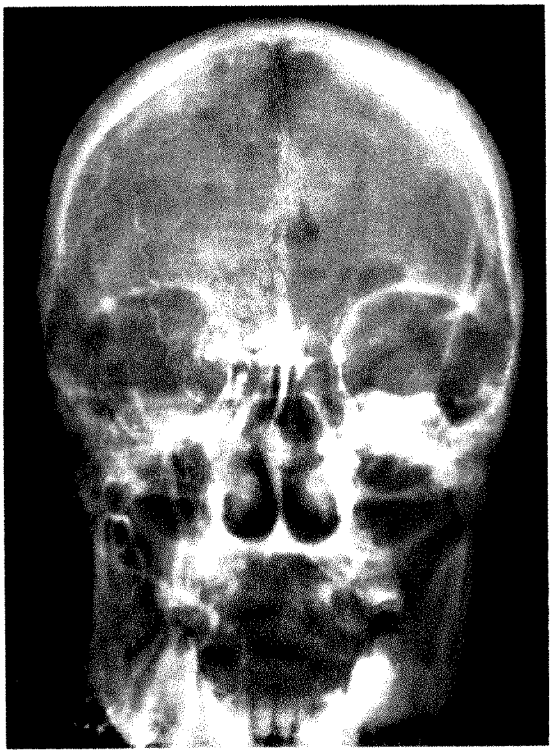


Fig. 4. Case I. Anteroposterior roentgenogram at $4\frac{1}{2}$ seconds. The vascular blush is poorly visualized above the superior inner margin of the orbit.



→

Fig. 6. Case II. There is a faint vascular blush above the inner margin of the orbit.

diencephalon and arise from the anterior cerebral artery or anterior communicating artery. The central telencephalic artery of Heubner usually arises from the anterior communicating, occasionally from the anterior cerebral artery itself, and supplies the caudate nucleus, the internal capsule, and the lenticulate nucleus. The posterior communicating artery supplies the hypothalamic arteries, about 6 in number, which originate along the course of the posterior communicating artery and supply the infundibulo-pituitary axis and mammillary region. The thalamic artery ascends to the thalamus. The posterior cerebral artery gives off a few small branches posteriorly via the hypothalamic artery.[1,2,3,4]

REPORT OF CASES

Case I. An 82 year old white male was admitted with a presumptive diagnosis of stroke. Physical examination demonstrated left hemiplegia but was otherwise unremarkable. A left carotid arteriogram made on the day of admission demonstrated an occlusion of the middle cerebral artery at its origin and apparent diminution of the flow through the anterior cerebral artery. The posterior communicating and posterior cerebral arteries filled well. A serial roentgenographic study revealed an increasing vascular blush about the region of the thalamus and basal ganglia which became more distinct toward the end of the arterial phase and was far more apparent on the lateral than on the anteroposterior roentgenograms (Fig. 1, 2, 3, and 4). The laboratory findings were within normal limits. The patient expired 9 days after admission. Autopsy revealed encephalomalacia of the temporal lobe and an occlusion of the left middle cerebral artery. There was no evidence of tumor.

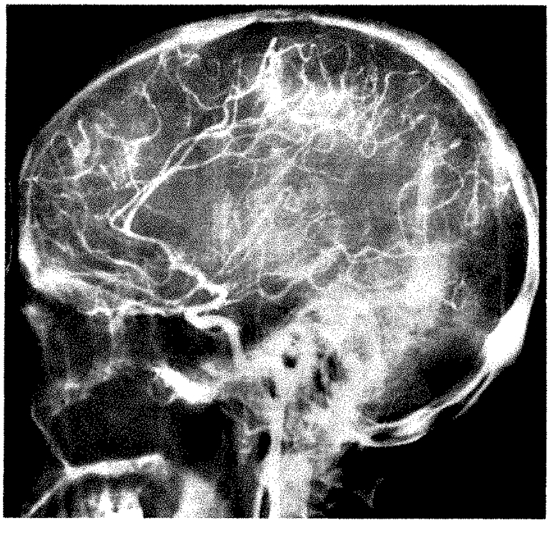


Fig. 7. Case III. Left lateral roentgenogram shows almost complete occlusion of the middle cerebral artery with occlusion of the ascending fronto-parietal branch. Note the vascular blush arising in the region of the posterior communicating branches.

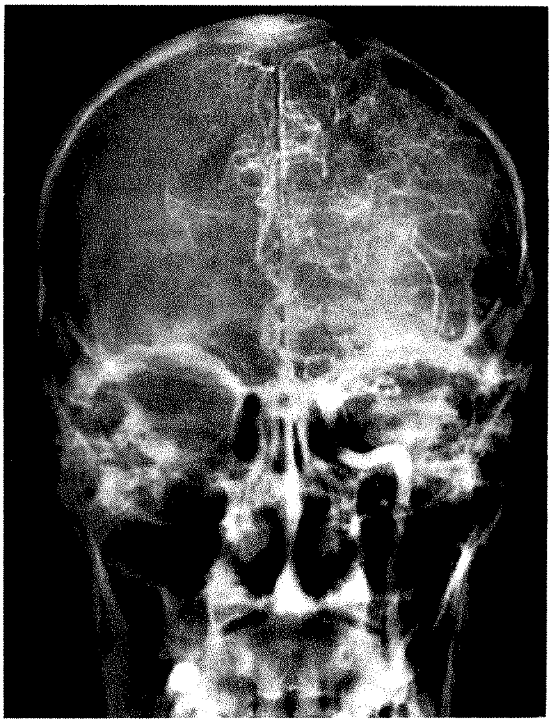


Fig. 8. Case III. Anteroposterior roentgenogram shows a slight shift of the anterior cerebral artery to the right. Slight blush is noted above the inner margin of the orbit.

Comment. The vascular blush raised the possibility of a deep-seated neoplasm. However, the internal cerebral vein was normally situated and the clinical picture could be adequately explained by the arterial occlusion. The postmortem examination confirmed the clinical diagnosis, indicating that the pseudotumor effect was indeed the normal blood supply to the basal ganglia and thalamus.

Case II. R.T., a 34 year old female, was admitted following a head injury with complaints

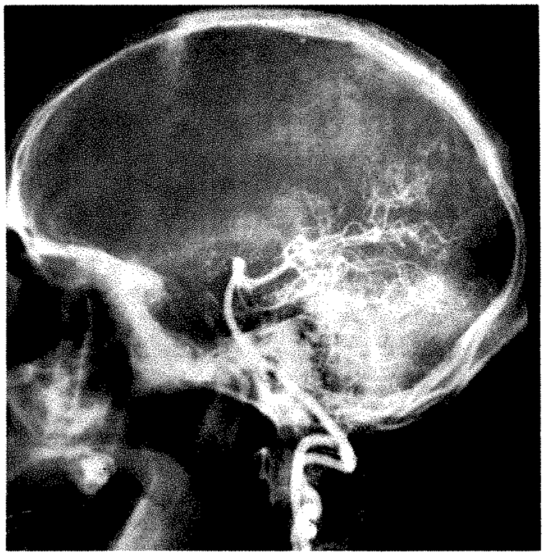


FIG. 9. Case IV. Lateral vertebral angiogram shows branches from the posterior cerebral vessels which cause a faint blush above the posterior cerebral vessels

of headache. There was a history of stroke 4 years previously with residual left hemiparesis. A right carotid angiogram was made and revealed an occlusion of the internal carotid at its bifurcation. A vascular blush, best seen in the lateral view and faintly visualized in the anteroposterior view just lateral to the midline, seemed to receive its blood supply from the posterior communicating artery. Because of the experience with the first case, we were aware that the blush was due to normal vascular supply to the thalamus and basal ganglia. The patient improved and left the hospital with residual hemiparesis (Fig. 5 and 6).

Case III. B.C., a 46 year old male, was unconscious on admission. He had a right hemiplegia. A left carotid arteriogram demonstrated partial occlusion of the middle cerebral artery with a delay in filling of the remaining branches. A slight vascular blush was seen in the region of the thalamus and basal ganglia. The anterior cerebral artery was slightly deviated to the right, but the venous angle and the internal cerebral vein on serial roentgenograms were in normal position. The patient improved and left the hospital with residual hemiparesis (Fig. 7 and 8).

Comment. The slight shift of the anterior cerebral artery was attributed to brain swelling and not to a deep-seated tumor in line with our previous cases.

Case IV. This patient was admitted with a hemiparesis which had been present for several months, with gradually progressive severity. Bilateral carotid angiograms, a pneumoencephalogram and a vertebral angiogram were obtained. All were within normal limits. Figure 9 demonstrates the thalamic distribution of the arteries arising from the posterior circulation.

DISCUSSION

The importance of knowledge of the normal vascular pattern is emphasized by these cases, particularly by Case III, where some indications for craniotomy were present.

SUMMARY

The normal central structures have a blush pattern which can mimic a tumor stain. The position and configuration of the internal cerebral vein and of the thalamostriate vein are of considerable importance in the evaluation of a vascular blush in this area.

Leon Love, M.D.
Department of Radiology
Cook County Hospital
Chicago 12, Illinois

REFERENCES

1. Gray, H. Anatomy of the Human Body. Twenty-sixth edition. Lea & Febiger, Philadelphia, 1954, pp. 641–644.
2. Krieg, W. J. S. Functional Neuroanatomy. Blakiston Company, New York, 1942, pp. 436–438.
3. Lazorthes, G., Poulhes, J., and Gaubert, J. Les artères et les territoires vasculaires de l'hypothalamus; applications neurochirurgicales. *Presse méd.*, 1956, *64*, 1701–1703.
4. Sherstennikov, E. N. Arteries of optic thalamus in man. *Arkh. anat.*, 1961, *40*, 91–95.

PANTOPAQUE ANTERIOR BASAL CISTERNOGRAPHY OF THE POSTERIOR FOSSA*

By HARVEY GASS, M.D.
DETROIT, MICHIGAN

ROENTGENOGRAPHIC visualization of the anterior portion of the posterior fossa is often unsatisfactory. Aside from plain roentgenograms of the skull in different projections and laminagraphy, one has available for this purpose vertebral-basilar angiography, ventriculography of the fourth ventricle and aqueduct by air or positive contrast material, and pneumoencephalography with full replacement technique or fractional pneumoencephalography to visualize the fourth ventricle, aqueduct and basal cisterns in the posterior fossa. These may still be inadequate for direct or indirect visualization of this area. Not much attention has been paid, however, to visualization of the posterior fossa basal cisterns by the use of positive contrast material such as pantopaque (Fig. 1, 2 and 3). Brown and Aye[1] in 1955 described the visualization of the vertebral-basilar arteries by pooling the pantopaque through the foramen magnum into the posterior fossa. Malis[2] described the myelographic examination of the foramen magnum as well as a technique for visualizing the basal cisterns with pantopaque and demonstrated some of the anatomic features of this area. His attention, however, was primarily directed toward visualizing lesions around the foramen magnum rather than in the anterior portion of the posterior fossa. Mones and Werman[5] described a technique called pantopaque myeloencephalography which was of particular value for lesions affecting the posterior portion of the foramen magnum and cisterna magna. In 1960, Mellins[4] reported on posterior fossa cisternography with pantopaque. Several pathologic lesions affecting the anterior cisterns of the posterior fossa were visual-

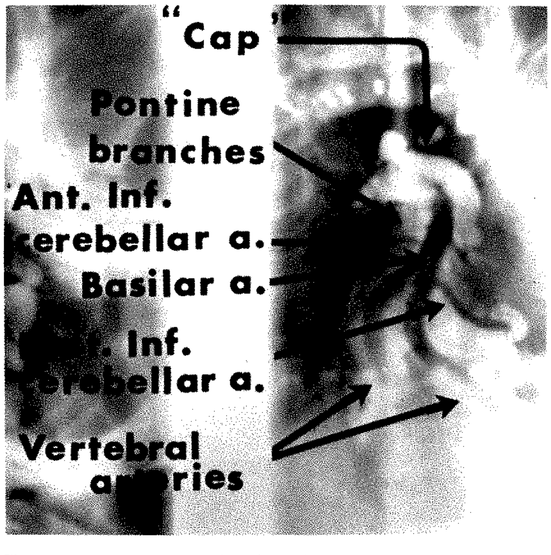


Fig. 1. Anteroposterior basal cisternogram through open mouth showing mildly tortuous vertebral-basilar arterial system. "Cap" indicates rostral limit of prepontine cistern.

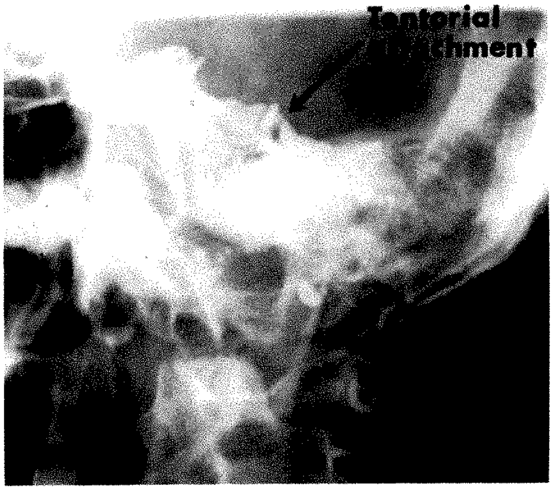


Fig. 2. A normal oblique roentgenogram of cerebellopontine cistern. No filling defects.

---

* From the Department of Neurosurgery, Wayne State University School of Medicine, Sinai Hospital and Mount Carmel Hospital, Detroit, Michigan.

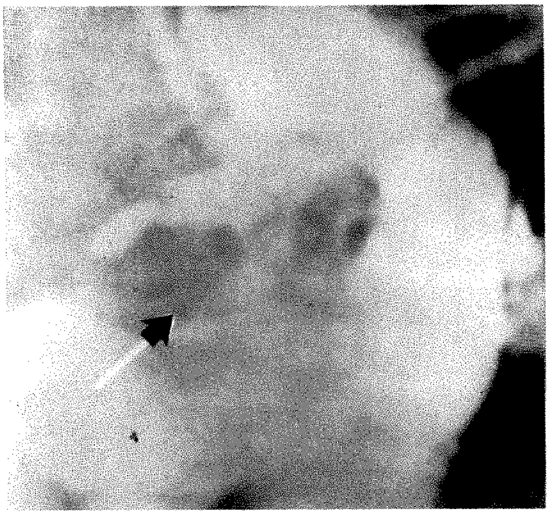


Fig. 3. Oblique roentgenogram of cerebellopontine cistern showing filling defect caused by acoustic neuroma.

ized by this technique.* The purpose of this paper is to re-emphasize this technique and to elaborate further on it.

Not only may cisternography occasionally reveal lesions difficult to identify roentgenologically in any other way (Fig. 4), but it may also provide information about the size and shape of certain lesions and, in some instances, the proximity of the lesion to the basilar artery. In certain cases, cisternograms may suggest by the corrugated edge of the contour of the lesion that its histologic nature is meningioma. Other information of value regarding the vertebral-basilar system and its pathologic disturbances may also be revealed. This may include aneurysms arising from these arteries, arteriosclerosis, and extreme tortuosity and redundancy of the arterial tree sufficient to irritate the eighth nerve complex.

The information obtained regarding pathologic lesions may be unequivocal, although inconclusive interpretations occasionally must be made and complete visualization of the anterior cisterns is not always possible. This does not detract from the value of the study, since the findings in positive cases are definite.

METHOD

The technique is safe. It consists essentially of pooling a quantity of pantopaque along the clivus up to the dorsum sellae in a controlled manner with fluoroscopic guidance and the taking of spot roentgenograms in the anteroposterior and right and left oblique projections. When a set of satisfactory roentgenograms has been obtained, the contrast material is allowed to gravitate to the lumbar subarachnoid space from which it can be removed. Before removing the contrast material a lateral roentgenogram is sometimes made which usually

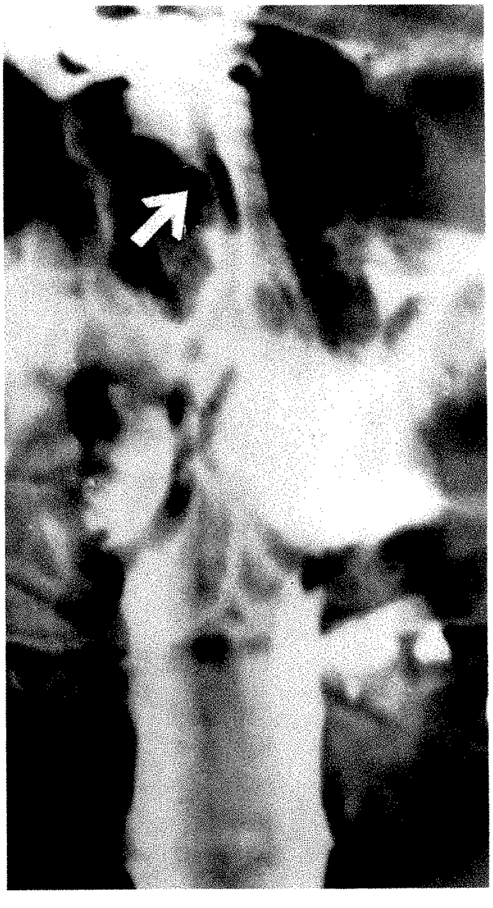


Fig. 4. Indentation in the prepontine cistern caused by unilateral enlargement of the pons due to astrocytoma, pathologically verified. At the time this study was made, fourth ventricle pneumoencephalography was within normal limits.

---

* In a few of these cases the procedure was performed by the author and they are included in this report.

shows a phalanx of the medium running from the foramen magnum or upper cervical spinal canal along the clivus to the dorsum sellae (Fig. 5). This study has not yet proved to be of diagnostic value and is often omitted.

The procedure is started by injecting about 12 cc. of pantopaque into the lumbar subarachnoid space and allowing it to pool into the cervical spinal canal, with the head of the patient in sharp hyperextension as is usual for cervical myelography. This large quantity of contrast medium in the cervical spinal canal makes it somewhat easier subsequently to collect a sufficient amount of the material in the posterior fossa for adequate roentgenograms, although, at times, when it is difficult to get this quantity in the cervical spinal canal, satisfactory roentgenograms may be obtained even with lesser amounts. Once the contrast material is accumulated in the cervical area, the tilt table is brought to the horizontal position and the medium is further advanced into the posterior fossa by short downward tilts of the table of about 10 to 15 degrees combined with the gradual tilt of the head toward flexion as needed to permit the material to run into the posterior fossa. Usually only one or two tilts of the table are needed since the contrast medium is carried rostrally mostly by the head flexion. Two operators are advisable, one to perform the fluoroscopy and one to control the rotation of the patient's head with gloved hands. With the head in hyperextension, the chin is brought to the table and the head is slowly flexed bringing the nose toward the table. The material can be seen to gravitate over the region of the dens where the column may break. It then runs quickly into the cistern overlying the clivus. Here it tends to collect once more. If too sharp a flexion of the head is required to achieve this, the head may be extended again and the table tilted downward another short distance. Then, once again, the head is flexed until the medium descends into the region of the clivus. This can be recognized by two features, either or both of which may be identifiable fluoroscopically. As the contrast medium accumulates over the clivus, a smooth sinuous curve begins to take shape, representing the outline of one or both vertebral arteries and/or the basilar artery and, as the droplets of medium collect into a pool, the contour of these vessels becomes identifiable. Secondly, if the flexion of the head is not too great, the pool of contrast material accumulating over the clivus assumes a natural limiting "cap" rostrally (Fig. 1), representing the forward limit of the advancement of the medium. Visualization of this area is often aided by fluoroscoping with the patient's mouth open.

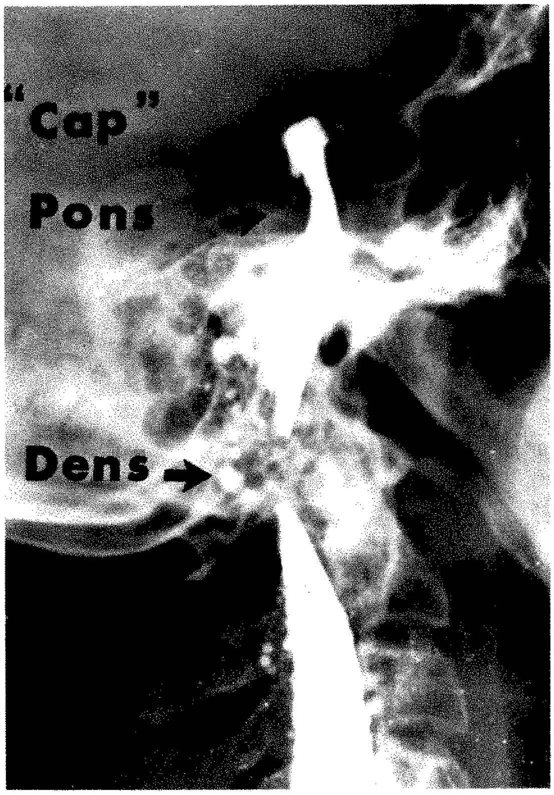


Fig. 5. Normal lateral anterior basal cisternogram.

If a mass is present in the posterior fossa, it may not be possible for a large quantity of medium to accumulate in the basal cisterns. There may be a partial block at the level of the herniated tonsils in the region of the foramen magnum or at the inferior edge of the tumor mass itself. In such instances,

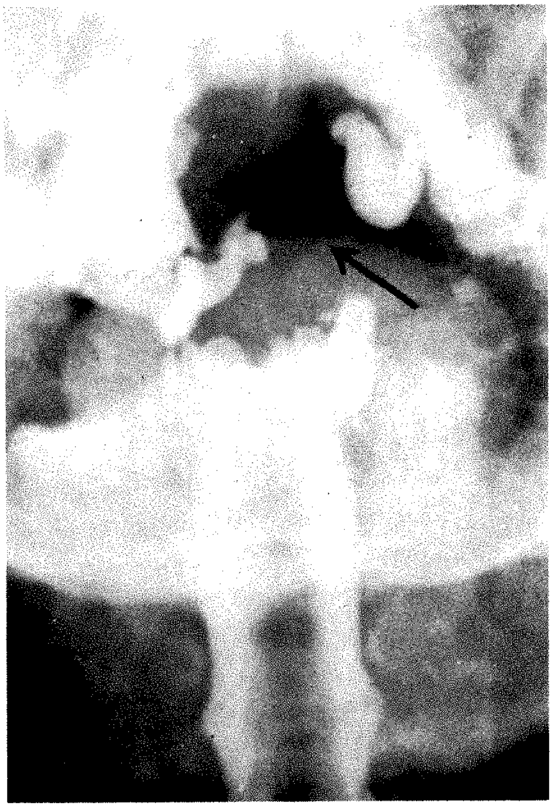


Fig. 6. Anteroposterior basal cisternogram in a patient with nasopharyngeal carcinoma eroding through the clivus into the posterior fossa. Arrow points to filling defect in prepontine cistern.

only a trickle of contrast material may enter the basal cisterns but, as a rule, even this small amount is sufficient to outline the vertebral-basilar arteries at least in part and/or the tumor edge, these being the most dependent structures projecting into the cistern. In other cases, only a small quantity may collect in the prepontine cistern at first, and may outline only one side of the vertebral-basilar system, thus raising the issue as to whether or not a mass on the opposite side prevents its accumulation there. With rotation of the head, however, as subsequently described, a small amount will then tend to reach both sides of the vertebral-basilar system. In the presence of a tumor of the clivus itself, incomplete filling of the prepontine cistern may result (Fig. 6). When a sizeable amount of pantopaque has accumulated in the cisterns overlying the clivus, under normal circumstances, the rostral "cap" and, silhouetted in the pool of pantopaque, the basilar artery and both vertebral arteries are visualized. In addition, varying extents of some of the branches arising from the system may be visible including the superior cerebellar, pontine, internal auditory, anterior inferior cerebellar, posterior inferior cerebellar, and anterior spinal arteries. The appearance of the basilar artery, both vertebrals, and paired branches arising from the basilar artery is that of a caricature of a "man without a head." If the vertebral-basilar system is unusually tortuous, it may be difficult at first glance to identify the component parts of the system. Anteroposterior spot roentgenograms are taken with the mouth either open or closed at this time. Then the head is rotated for oblique views. Maintaining the degree of extension necessary to outline the "cap", combined with the appropriate contralateral flexion of the neck, the head is rotated with the occiput to one side, causing the contrast material to flow toward the cerebellopontine angle. There is little fear of losing the medium above the tentorium with this maneuver because the attachment of the tentorium to the petrous ridge contains it within the posterior fossa. It is important to turn the head as far as possible even if it is necessary to rotate the patient's body into the lateral position. This enables visualization of the cerebellopontine cistern as completely as possible. When these roentgenograms are made, the head is again turned back to the anteroposterior position being certain to maintain the previous degree of extension so as not to lose the opaque medium. The medium will return to the prepontine cistern. The head is then rotated towards the opposite side in the same manner and comparable roentgenograms are obtained. Such oblique roentgenograms may show a limiting edge, sometimes straight, representing the attachment of the tentorium to the petrous ridge

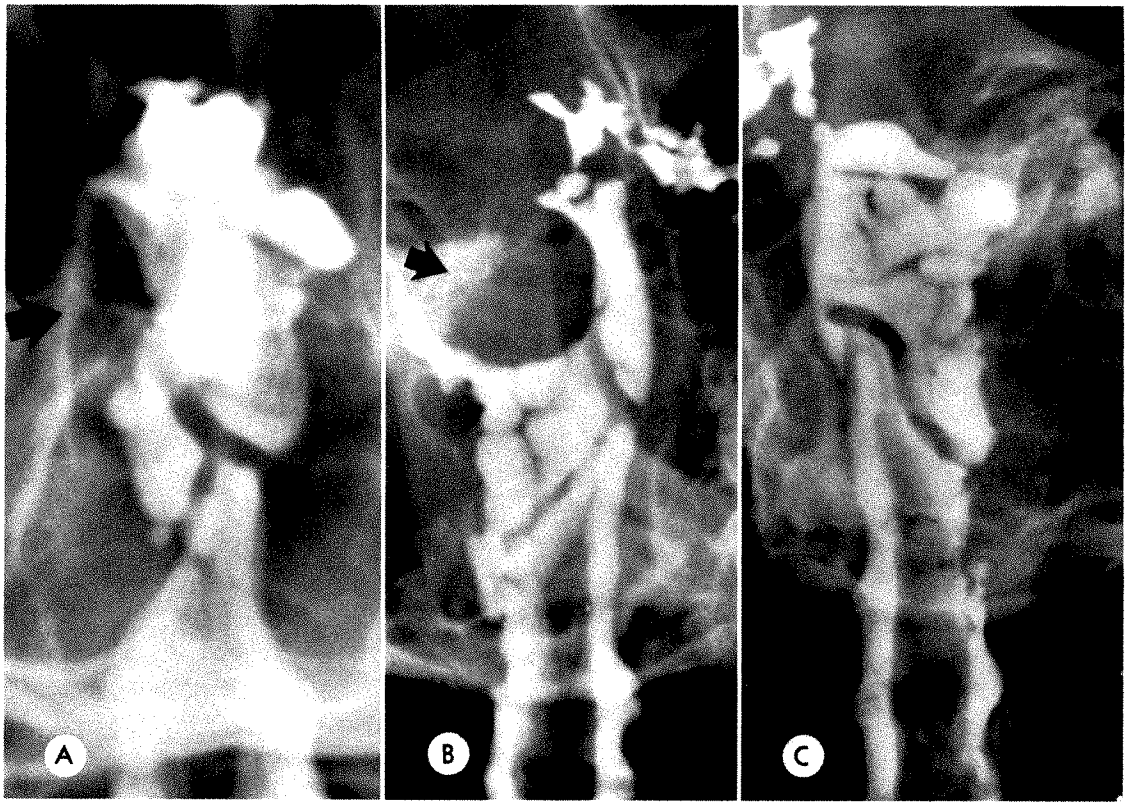


FIG. 7. (*A*) Anteroposterior roentgenogram showing indentation in the prepontine cistern (arrow). (*B*) Left oblique view showing the indentation as a globular defect (arrow) which is unequivocal, particularly when compared with (*C*) the right oblique roentgenogram. The defect proved to be due to a meningioma in the angle. The solitary manifestation of this patient's tumor was numbness in the left side of the face of six months' duration. Fractional pneumoencephalography was negative with the exception of a cut-off of the air in the cerebellopontine angle on the left side (Fig. 8). There was no displacement of the fourth ventricle.

for a variable distance. They also show varying lengths of branches of the vertebral-basilar system traversing the cerebellopontine cistern. If these cisterns fill well with pantopaque and there is no filling defect or a globular indentation, it may be assumed that no mass is present in this area (Fig. 2). If on the anteroposterior roentgenogram a tumor mass is suggested, its contour may be further clarified or accentuated on the oblique roentgenograms (Fig. 7, *A–C*). Tumor masses tend to be globular and, therefore, produce a round indentation of the pantopaque silhouette. The proximity of the edge of the tumor to the basilar artery may be seen on the anteroposterior roentgenogram and may be of subsequent technical help to the operator (Fig. 7, 10 and 11). Several meningiomas visualized in this manner have shown a lobulated edge, presumably as a result of the raspberry-like surface of the tumor (Fig. 9, 10 and 11).

There is considerable variability in the size of the cisterns and, if small, the extent of the cerebellopontine cistern filling may be limited. In such circumstances, it may be somewhat difficult to be certain that limitation is not due to a tumor edge. Therefore, unless a sharp globular shadow is visible on one side which is not comparably present on the other side, one should be doubtful about making the diagnosis of a mass lesion. At times, progress roentgenograms in doubtful cases taken several

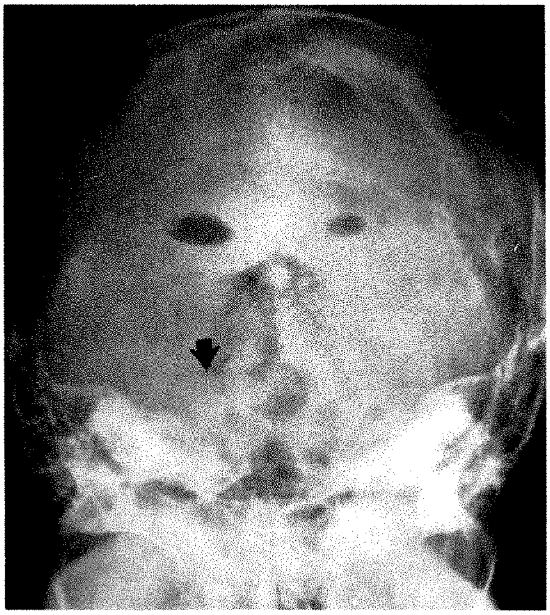


Fig. 8. Pneumoencephalogram of same patient as in Figure 7 showing the only positive finding, a cut-off of the air in the cerebellopontine angle on the left side (arrow).

months apart may reveal a change in the outline, indicative of a growing process (Fig. 12, *A* and *B*). If the cerebellopontine cistern is large, a tumor therein may not obliterate but create a filling defect (Fig. 3).

LOSS OF CONTRAST MATERIAL

If the contrast material is allowed to pass beyond the rostral "cap", it flows through the incisural notch and enters the supratentorial area and is lost above and beside the sella turcica and into the anterior and middle fossae. If this happens, the patient usually experiences a sudden frontal headache. This indicates to the operator that the head should again be extended to avoid losing more medium. Losses of contrast material tend to occur when the head is flexed too abruptly and too far. The ability of the patient to cooperate with the operators determines the ease with which this part of the study may be satisfactorily accomplished. At the beginning of the intracranial examination, the patient should be instructed to permit the operator to make all motions of his head passively and not to speak.

After satisfactory roentgenograms have been obtained, the table is brought upright with the patient's head in hyperextension and the medium is allowed to gravitate to the lumbar sac from which it can be removed. If no material has been lost above the "cap", all of it can be recovered but occasionally a drop or two may be left in the lateral cisterns of the posterior fossa. If some material has been lost above the tentorium, by maintaining the patient in the upright position with sharp hyperextension of the neck and lumbar spine and

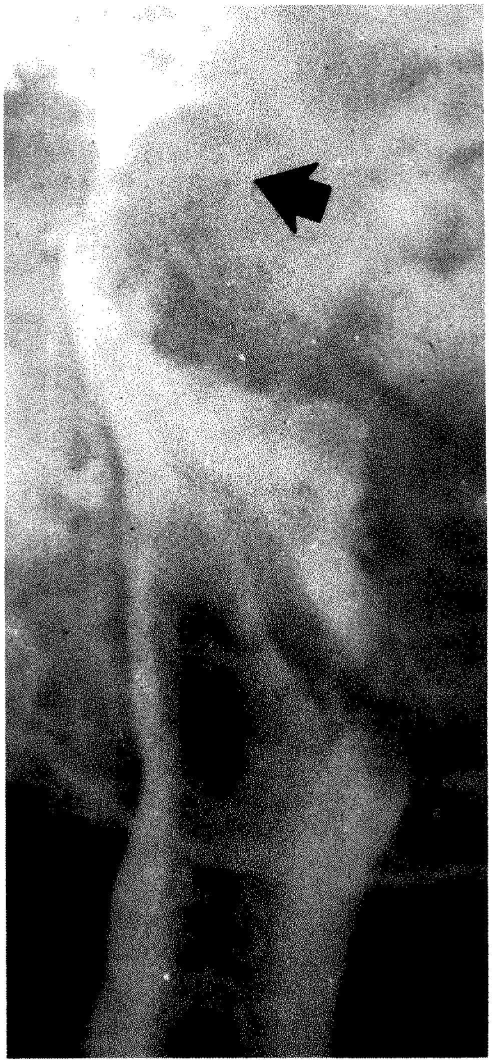


Fig. 9. Oblique roentgenogram showing the globular indentation of angle meningioma. Arrow points to lobulated edge characteristic of meningioma.

rotating the head in several directions, a significant amount may also be recovered. The lost contrast material seeps into the subarachnoid spaces and not along the ependymal lining of the ventricular system. As has been reported by Wright,[6] subsequent pneumoencephalography may further reduce the amount of "lost" medium in the supratentorial compartment. Rarely is more than 0.5 to 1 cc. of the contrast material lost and we have never experienced any late ill effects from this. We have deliberately not utilized the supratentorial pantopaque to visualize suprasellar lesions, but this would be feasible in selected cases where it might be important to obtain information about this area which otherwise would not be available. We concur with Malis[2] that the fear of retained medium in the head, especially the small quantities involved here, is not realistic. The occasional report of severe reactions, even if causally related to the presence of contrast material in the head, must represent a hypersensitivity of the patient to the medium. There is little or no concern about retained droplets of the medium in the lumbar cul-de-sac which cannot be removed after routine myelography. When one makes the decision to do even lumbar myelography, he accepts such a loss as part of the small calculated risk of performing this examination. Undoubtedly, retained droplets of pantopaque in the head are seen with great frequency on skull roentgenograms of patients who previously have had myelographies and such findings are assumed to be asymptomatic. A patient who has an idiosyncrasy, as in the case of Mason and Raaf[3] or those reviewed in their article, may have a severe reaction if only lumbar myelography is done. Inasmuch as most of the time complete recovery of the contrast material is the rule in this examination, occasional

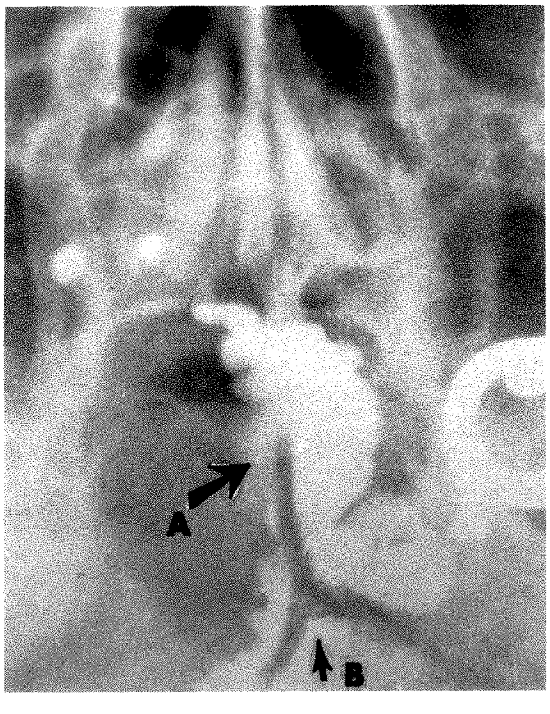


Fig. 10. Anteroposterior roentgenogram showing edge of meningioma (arrow A). Arrow B indicates vertebral basilar system and its proximity to the tumor edge (slightly retouched).

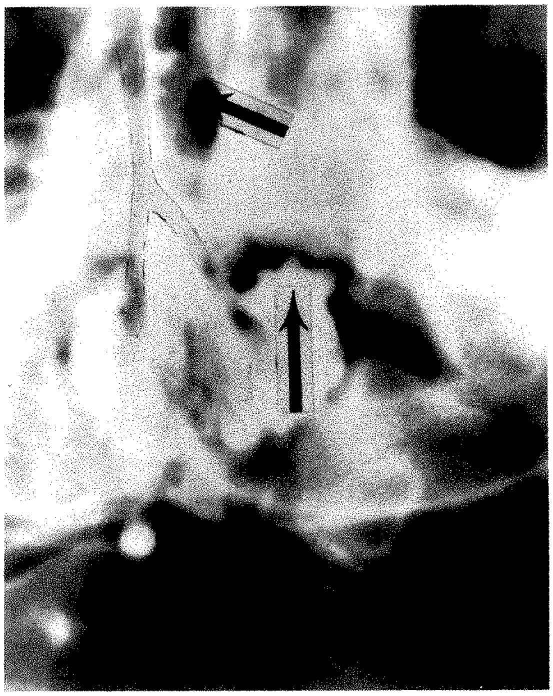


Fig. 11. Anteroposterior roentgenogram showing only a small trickle of medium reaching the prepontine cistern but which is sufficient to outline the lobulated edge of a meningioma (upper arrow). Most of the medium is blocked from gaining access to the prepontine cistern by the inferior edge of the tumor (lower arrow) (slightly retouched).

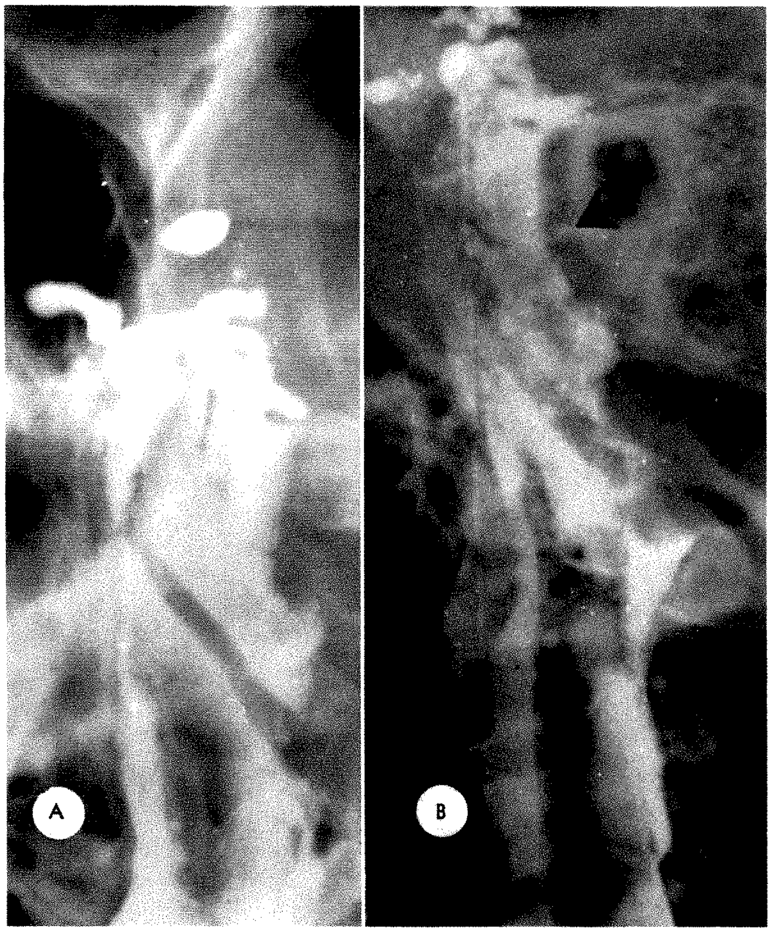


FIG. 12. (*A*) Right oblique roentgenogram showing poor filling of the cerebellopontine angle but no definite tumor edge. (*B*) Six months later a distinctly different contour is seen, representing the smooth edge of an acoustic neuroma (arrow).

loss of a small quantity does not seem to be a contraindication to its performance.

SUMMARY

The possibility of identifying lesions in the cerebellopontine angle early and gaining information about their size, their relationship to the basilar artery and possibly even about their type favors the use of pantopaque cisternography. Surgical results of operable cases are presumed to be better when the lesions can be identified early, and complete removal is more likely.

529 Fisher Building
Detroit 2, Michigan

REFERENCES

1. Brown, F. M., and Aye, R. C. Myelographic demonstration of basilar artery. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1955, *73*, 32–34.
2. Malis, L. I. Myelographic examination of foramen magnum. *Radiology*, 1958, *70*, 196–221.
3. Mason, M. S., and Raaf, J. Complications of pantopaque myelography; case report and review. *J. Neurosurg.*, 1962, *19*, 302–311.
4. Mellins, H. Z. Diagnosis of lesions in the basilar artery, pons and cerebellum by high cervical myelography. Report to the Radiological Society of North America, Cincinnati, December 6, 1960.
5. Mones, R., and Werman, R. Pantopaque myeloencephalography. *Radiology*, 1959, *72*, 803–809.
6. Wright, R. L. Removal of residual intracranial pantopaque by pneumoencephalography. *J. Neurosurg.*, 1961, *18*, 831–833.

CONVENIENT PNEUMOENCEPHALOGRAPHY

By A. D. SEARS, M.D.
DALLAS, TEXAS

INCREASING reliance upon upright roentgenography during pneumoencephalography, especially for posterior fossa studies, has prompted progressive improvement in the technique of supporting unconscious patients. The equipment consists of variations of an open back chair,[2] a simple support on an ordinary stretcher,[4] a parachute harness,[3] and a sack-like canvas bag attached to the ceiling.[5] More complex and expensive to use are the difficult-to-store orthopedic frame, the somersaulting chair, and the serviceable Swedish chair-couch.[1]

After much experimentation, an inexpensive hydraulic therapy couch* has been modified for pneumoencephalography (Fig. 1, *A* and *B*). Similar to the Swedish chair-couch, it provides excellent support for an unconscious patient and frees personnel during roentgenography. The couch is easily movable and one lever locks all wheels. The footboard end is used with a Franklin head unit, the opposite end with the Lysholm skull table. The device is compact and easily stored. It is also useful for decubitus roentgenography against an upright roentgenographic table, particularly during cholecystography.

The outstanding advantage of this unit

---

* Reliance Therapy Couch, manufactured by F. F. Koenig-Kramer Co., 96 Caldwell Drive, Cincinnati, Ohio.

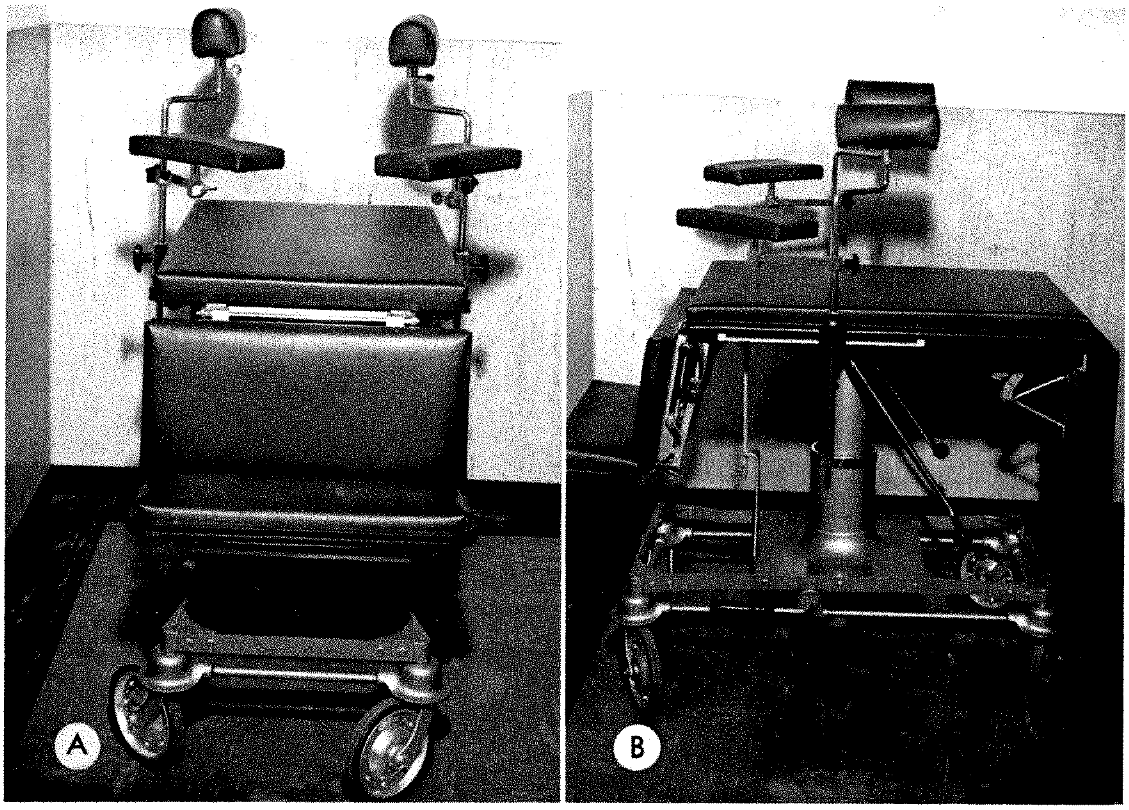


Fig. 1. (*A*) Front view and (*B*) side view of couch showing adjustable features of axillary and forearm supports.

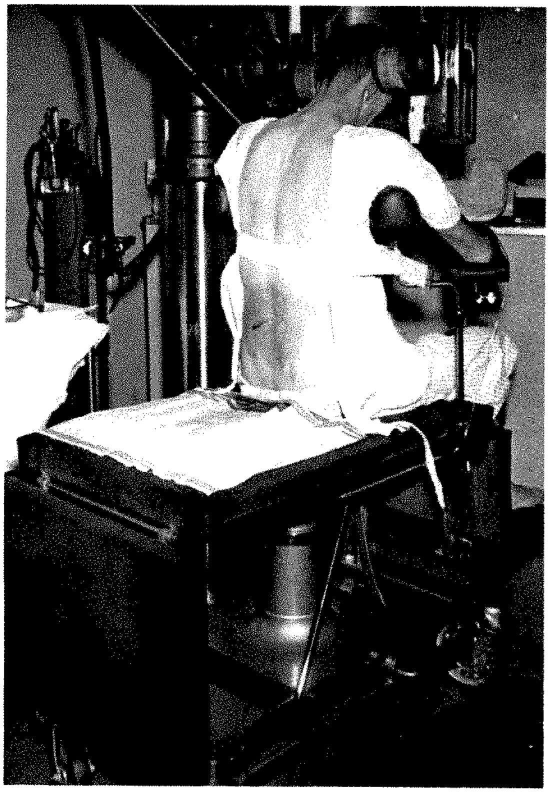


FIG. 2. Patient in position for axial roentgenograms of posterior fossa.

during pneumoencephalography is the minimal patient movement once the head is positioned over the folding end. By supporting the head as the end folds, easy positioning on the skull table is effected. The patient may be taken to his room after the study without being transferred from the couch. The neurosurgeon is comfortable during the procedure because of the compactness of the device when both ends are folded. Hydraulic elevation provides a comfortable working height and easy adjustment of the patient's head.

METHOD

The patient sits on the stretcher in an erect position, supported if necessary. The "crank-shaped" axillary support bars are rotated medially or laterally to adjust for patient width, then adjusted along the bar parallel to the table top to center the cushions under the axillae. The cushions are raised into the axillae and clamped. The forearm supports are adjusted for height, rotated medially or laterally as needed, and locked. Cushions also rotate to fit the forearm angle. A web belt around the patient and the upright supports provide increased stability. The procedure consumes 3 to 5 minutes.

After the patient is anesthetized, the head is supported erectly and the entire unit is moved to the skull table. The head is positioned and fixed with clamps or a compression band and the stretcher is locked (Fig. 2). A spinal puncture is performed, and small injections of air are checked with a Polaroid camera. Neck flexion is adjusted by simply unlocking and pulling or pushing the couch away from, or toward, the unit. For lateral roentgenograms (Fig. 3), the entire skull table and roentgen-ray tube are unlocked and slid

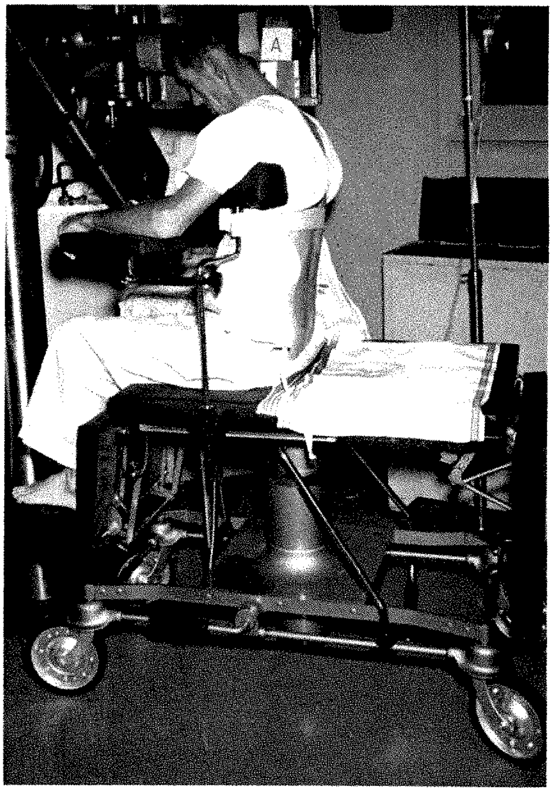


FIG. 3. Patient in position for upright lateral roentgenograms. Skull table (A) is unlocked and shifted away from support to allow space for footboard.

away from the main support column as far as possible. This provides additional space for the carriage and permits easier erect positioning so that more of the cervical area is demonstrated.

After upright roentgenography, the patient is briefly held while the belt and supports are removed, then gently lowered into the supine position with the head and shoulders over the folding end for anteroposterior roentgenograms. The remaining routine and special roentgenograms, if needed, are taken in sequence. In an uncomplicated case, a complete study with stereoroentgenography requires 45 minutes or less.

For infants we use an ordinary "Easy Infant Positioner,"* without legs on one end of the stretcher (Fig. 4). The unit supports an unconscious child easily, being adjustable in height and width and having padded depressions for the axillae. Using the couch merely facilitates moving the patient from one position to another.

SUMMARY

1. An inexpensive modified therapy couch for use during pneumoencephalography is described.
2. The couch provides excellent support for unconscious, upright patients, and is easy to move and stabilize.
3. The unit is adaptable to the majority of skull tables in use and permits a marked decrease in patient handling.
4. The couch is especially useful for decubitus roentgenography against an upright table.

Department of Radiology
Baylor University Medical Center
Dallas, Texas

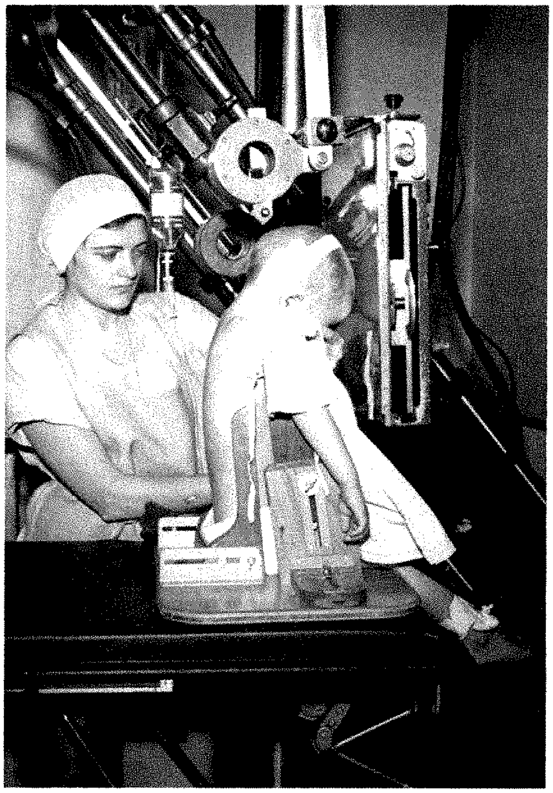


FIG. 4. Infant positioner (without legs) demonstrating use during combined pneumoencephalography and ventriculography.

REFERENCES

1. LINDGREN, E. Convertible chair-couch for roentgen examinations. *Acta radiol.*, 1961, *55*, 369–373.
2. ROBERTSON, G. Pneumoencephalography. Charles C Thomas, Publisher, Springfield, Ill., 1957, pp. 73–75.
3. SCHECHTER, M. M., and STRENGER, L. Three simple devices to facilitate contrast neuroroentgenography. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1962, *87*, 363–365.
4. SCOTT, M. Technique for air encephalography using stretcher with detachable support for sitting position. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1962, *88*, 21–23.
5. SWANN, G. F. Recent advances in neuroradiology. *Postgrad. M. J.*, 1961, *37*, 385–411.

---

* Manufactured by Specialty Mfg. Co., 3026 Q St., Sacramento, California.

CERVICAL DISKOGRAPHY

A HELP OR HINDRANCE IN EVALUATING NECK, SHOULDER, ARM PAIN?*

By RALPH R. MEYER, M.D.†
SALT LAKE CITY, UTAH

PATIENTS with chronic neck pain, often with radiation into the shoulder and arm, are frequently seen in clinical practice. Although symptoms may be severe, objective findings are commonly absent or minimal. These symptoms may arise spontaneously or may follow trauma. Injury if it occurs may be of many types and many degrees of severity. The patient may have been in an automobile accident where his vehicle was struck from behind causing a sudden forcible extension and flexion of the neck, the so-called "whiplash injury." A precise diagnosis may then be important not only for the patient's physical well-being but also for medical-legal reasons.

Plain roentgenograms of the cervical spine are frequently not helpful for they may be normal even when the symptoms are severe. Osteochondrosis, consisting of narrowed intervertebral disks and marginal vertebral body osteophytes may be demonstrated. When these changes are present, it is tempting to use them as an explanation for symptoms. Unfortunately, they are extremely common; their frequency increases with age; are nearly universal past the age of 60; and are seen more often in patients

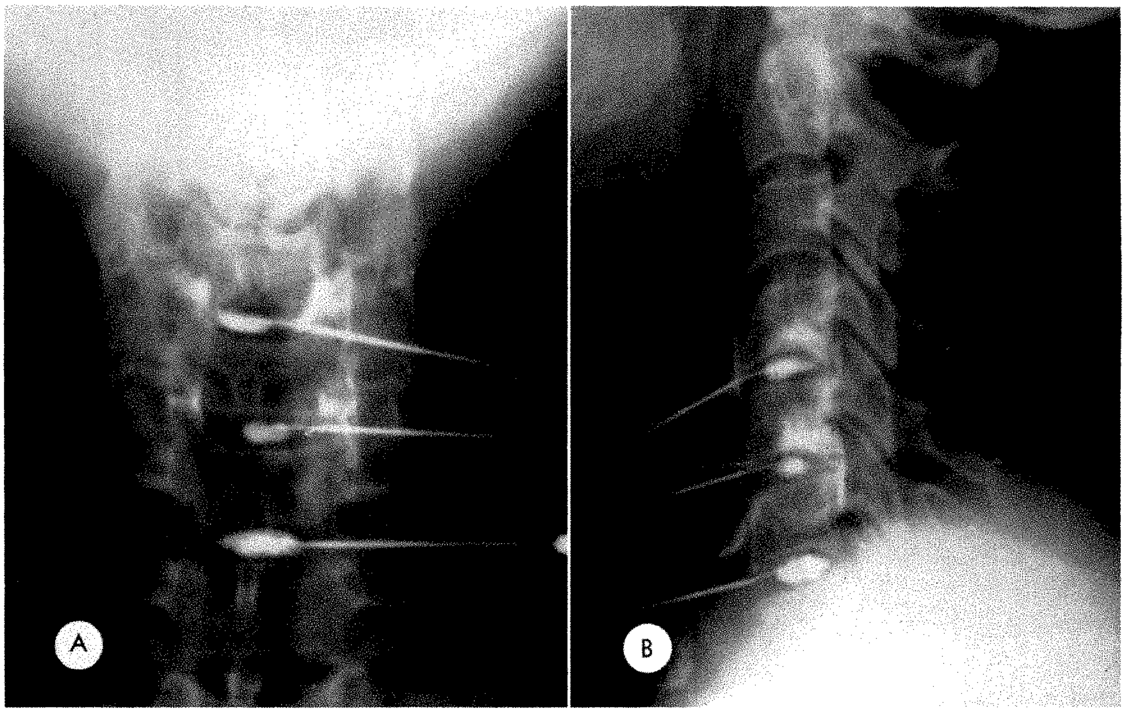


FIG. 1. Case J.E., aged 28. (*A* and *B*) Cervical diskograms illustrating normal nuclei at all three disk levels. C6–7 shows a normal disk; C4–5 and C5–6 levels show dissemination of contrast medium outside of disks anteriorly, laterally and posteriorly. Interpreted as possible disk disorganization at C4–5 and C5–6.

---

*From the Department of Radiology, Holy Cross Hospital, Salt Lake City, Utah.

† Associate Clinical Professor of Radiology, University of Utah School of Medicine.

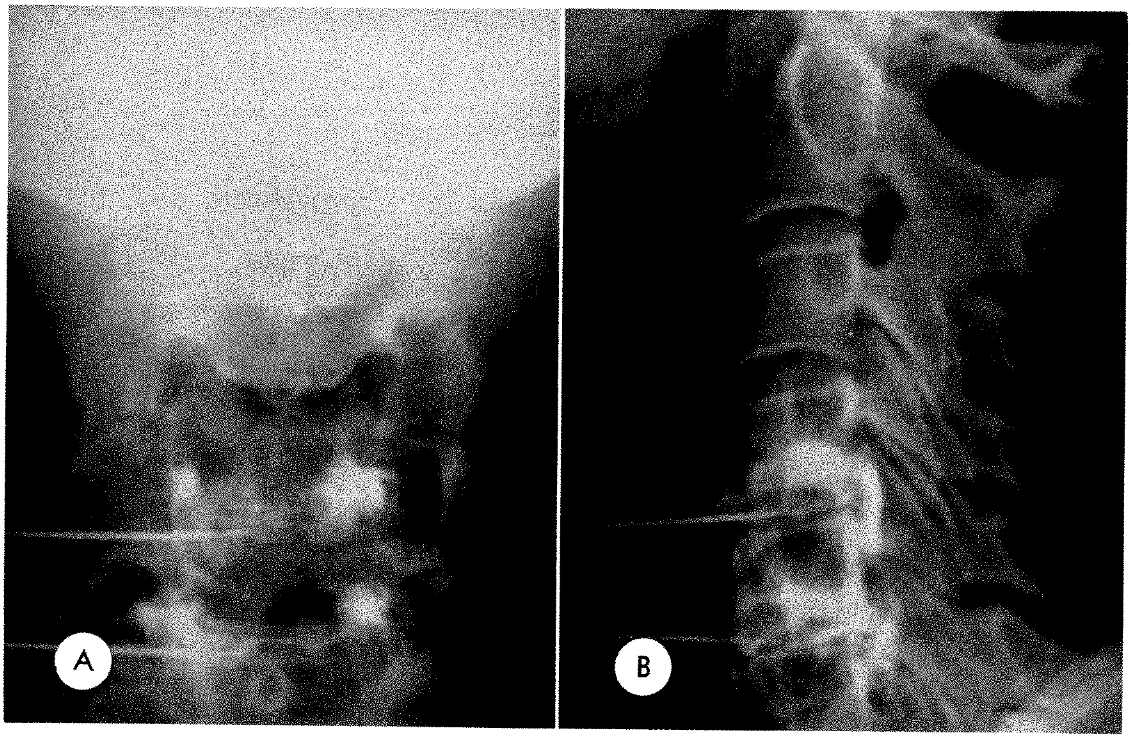


Fig. 2. Case F.H. (*A* and *B*) Cervical diskograms at C4–5 and C5–6. There is nonvisualization of nuclei, widespread extravasation through the disks, and extension into lateral recesses and posteriorly. Posterior extension may be into epidural space or represent projection of contrast medium in lateral recesses. Interpreted as possible disk degeneration with rupture of annulus.

without symptoms than in those with symptoms.[4]

Cervical myelography, though it might reveal unequivocal evidence of a protruding disk, more often is negative. Sometimes the impressions of the posterior vertebral body osteophytes on the subarachnoid space may be seen. This is only an additional manifestation of osteochondrosis and may not correlate with the patient's symptoms or signs.

Cervical diskography has been developed on the premise that neck, shoulder, or arm pain is due to disease of the intervertebral disk, which is not satisfactorily demonstrated by conventional roentgenographic techniques. Those[2,3,5] advocating diskography cite as its advantages simplicity of the procedure, reproduction of the patient's symptoms during the injection of the disk, and direct visualization of the disk. It is claimed that contrast studies of the disk will show whether or not the annulus is intact and may also show herniations of the disk not visible on myelograms.

Cervical diskography was performed in this department in an effort to obtain additional information as to the cause of intractable neck, shoulder, or arm pain. After reading the cervical diskograms of over 30 patients and finding it difficult to interpret any of these as normal, we became skeptical of the value of diskography. We thought it might be useful to present our experience particularly since the literature seems generally favorable to the method.

TECHNIQUE

Diskography may be defined as roentgenographic visualization of an intervertebral disk after the injection of an opaque solution into it. It was first used in the lumbar region,[1] more recently employed in the cervical spine.

TABLE I

FINDINGS IN 32 CERVICAL DISKOGRAPHIES

Patient	Sex	Age	Disks Injected	Result
E.I.	M	51	C3–4, C4–5, C5–6	Widespread extravasation at all levels into the right lateral recess
M.S.	M	35	C5–6, C6–7	C5–6—Widespread extravasation to the right and posteriorly into epidural space C6–7—Poor visualization
V.R.	M	43	C5–6, C6–7	C5–6—Extravasation from disk into epidural space C6–7—Normal nucleus
K.M.	M	42	C6–7	Widespread extravasation through disk into right lateral recess, precervical soft tissues, posteriorly into epidural space
M.O.	F	43	C5–6, C6–7, C7–D1	C5–6 and C6–7—Widespread extravasation bilaterally into lateral recesses C7–D1—Normal nucleus
C.B.	M	39	C4–5, C5–6, C6–7	C4–5—No visualization C5–6—Partial dispersion of medium within disk, no nucleus visualization C6–7—Widespread extravasation through disk
H.V.	F	35	C4–5, C5–6, C6–7	C4–5 and C5–6—Widespread extravasation through disks, precervical soft tissues, right Luschka's joints, and lateral recesses. Nuclei partially outlined C6–7—Normal nucleus
L.F.	M	55	C4–5, C5–6	C4–5—No visualization C5–6—Widespread extravasation into both lateral recesses and posteriorly. Posterior extension interpreted as herniated nucleus.
K.S.	M	37	C4–5, C5–6	C4–5 and C5–6—Widespread dissemination through disks with extension into epidural spaces. Possible posterior herniation at C4–5
J.E.*	F	28	C4–5, C5–6, C6–7	C4–5 and C5–6—Widespread extravasation outside of disks. Nuclei outlined C6–7—Normal nucleus
E.N.	F	48	C4–5, C5–6	C4–5 and C5–6—Widespread extravasation through disks and posteriorly into epidural space
D.S.	M	47	C4–5, C5–6	C4–5 and C5–6—Widespread extravasation through disks, extension into lateral recesses and posteriorly
R.K.	F	41	C5–6	C5–6—Widespread extravasation through the disk and posteriorly into epidural space
D.P.	M	15	C4–5	C4–5—Extravasation through right side of disk into right lateral recess

* Illustrated in Figure 1, *A* and *B*.

Table I (*Continued*)

Patient	Sex	Age	Disks Injected	Result
R.B.	M	50	C3–4, C4–5	C3–4 and C4–5—Widespread extravasation through disks, extension into soft tissues laterally and posteriorly, possible posterior herniation at C3–4
E.C.	F	43	C4–5, C5–6	C4–5 and C5–6—Widespread extravasation through and around disks, greater toward left
A.M.	F	43	C4–5, C5–6, C6–7	C4–5, C5–6 and C6–7—Widespread extravasation through all three disks, lateral and posterior extension into epidural space
F.L.	M	55	C5–6, C6–7	C5–6 and C6–7—Widespread extravasation with extension into right lateral recess and posteriorly into epidural space
R.F.	F	52	C5–6, C6–7	C5–6—Widespread extravasation, lateral and posterior extension C6–7—No visualization
C.J.	F	32	C4–5, C5–6	C4–5—No visualization C5–6—Extravasation to left and posteriorly into epidural space. Nucleus visualized
F.P.	F	34	C4–5, C5–6	C4–5 and C5–6—Extravasation with extension into right lateral recess. Nucleus outlined at C5–6
E.D.	F	48	C3–4, C4–5	C3–4—Extravasation through anterior two-thirds of disk, extension anteriorly C4–5—Extravasation through right lateral and posterior portion of disk, possible posterior disk protrusion
D.D.	M	35	C5–6	C5–6—Widespread extravasation, extension into lateral recesses and into epidural space
J.E.†	F	26	C4–5, C5–6	C4–5—Extravasation through right side of disk, extension posteriorly into epidural space C5–6—Widespread extravasation, extension into left lateral recess and posteriorly possibly into epidural space
J.W.	F	27	C4–5, C5–6, C6–7	C4–5—Extravasation through the right side of the disk, extension to the right and posteriorly into epidural space. Nucleus outlined C5–6 and C6–7—Normal nuclei
P.M.	F	21	C4–5, C5–6, C6–7	C4–5 and C5–6—Extravasation through right side of both disks, extension into right lateral recess, posterior extension at C4–5 C6–7—Normal nucleus
J.L.	M	45	C5–6, C6–7	C5–6 and C6–7—Widespread extravasation with extension into precervical soft tissues. Some posterior extension at C6–7

† Illustrated in Figure 3, *A* and *B*.

TABLE I (*Continued*)

Patient	Sex	Age	Disks Injected	Result
C.M.	M	14	C4–5, C5–6	C4–5—Widespread extravasation through the disk C5–6—Widespread extravasation through the disk and posterior extension into epidural space
G.B.	M	37	C3–4, C4–5, C5–6, C6–7	C3–4, C4–5, C5–6 and C6–7—Normal nuclei outlined at all levels, some epidural extension posterior to C3, 4, 5. Bilateral extension into lateral recesses at C3
R.M.	M	41	C5–6, C6–7	C5–6 and C6–7—Widespread extravasation, extension to the right, posteriorly, and into precervical soft tissues
F.H.‡	F	54	C4–5, C5–6, C6–7	C4–5 and C5–6—Widespread extravasation, extension into lateral recesses, posteriorly probably into epidural space C6–7—Nonvisualization
G.L.	F	26	C6–7, C7–D1	C6–7—Extension into epidural space. Normal nucleus C7–D1—Normal nucleus.

‡ Illustrated in Figure 2, *A* and *B*.

With few exceptions, all cervical diskographies in this department were performed by neurosurgeons who had carefully studied the procedure. The method was essentially the same as used elsewhere.[2,3] Needles were inserted into the disk from its anterolateral surface using a two needle technique. A No. 20 gauge needle was first placed diagonally into the outer anterolateral fibers of the annulus. Through this guide a No. 25 gauge needle was inserted into the nucleus which lies in the center of the disk. The position of the needle was determined by roentgenograms in two planes using anteroposterior and cross-table lateral views. When the tip of the needle lay near the center of the disk, the position was considered satisfactory and the contrast medium was injected with a syringe. A water soluble medium commonly used for intravenous urography, hypaque 50 per cent, proved quite satisfactory for disk visualization. Generally, not less than 0.2 cc. nor more than 1.0 cc. of hypaque was injected into the disk. After injection, anteroposterior and cross-table lateral roentgenograms were again made with the needles in place. If the roentgenograms were satisfactory, the needles were withdrawn and the examination was completed.

INTERPRETATION

According to the literature, a normal disk is one where the contrast medium is confined to the nucleus which appears as a central globule. The normal disk will accept 0.2 cc. to 0.3 cc. of solution. A pathologic disk will accept 0.5 cc. to 1.5 cc. of contrast medium. This will be dispersed through the disk often without outlining the nucleus. Dispersion frequently is generalized but may be localized to a portion of the disk. The contrast medium may pass beyond the confines of the disk into the surrounding soft tissues, and on into the lateral recesses or the epidural space. It is claimed[2] that contrast medium, projecting posterior to the disk in a hump-shaped fashion, indicates an extension of the nucleus pulposus into the spinal canal.

In our series diskograms were made of 32 patients of equal sex distribution, their ages ranging from 14 years to 55 years. A summary of our findings is shown in Table 1.

In Figure 1, *A* and *B* are diskograms showing normal nuclei. Figures 2, *A* and *B* and 3, *A* and *B* are examples of the usual appearance of diskograms in our series. Figure 4, *A* and *B* are roentgenograms of the cervical spine of a skeleton, showing how contrast medium in the lateral re-

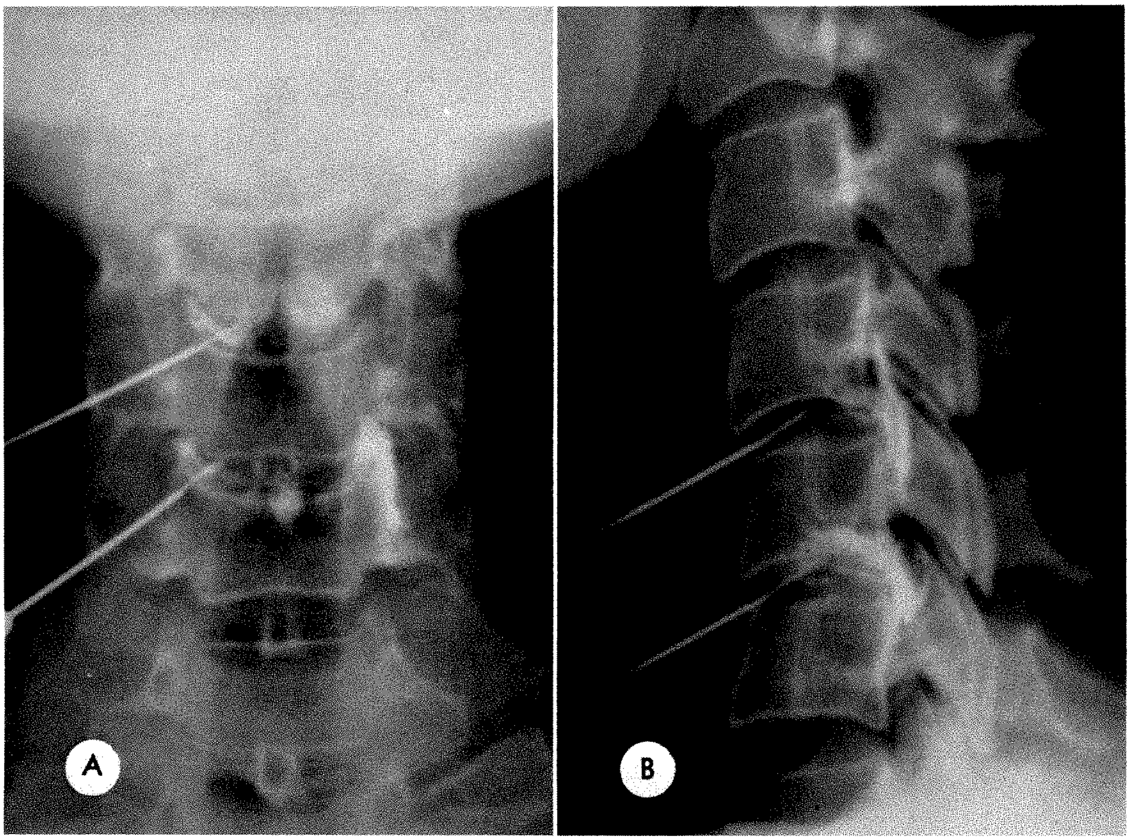


Fig. 3. Case J.E., aged 26. (*A* and *B*) Cervical diskograms at C4–5 and C5–6. There is nonvisualization of nuclei, extravasation through right side of disk at C4–5 with posterior extension into epidural space, widespread extravasation through the disk at C5–6, extension into the left lateral recess and posteriorly, possibly into epidural space or a projection of contrast medium in left lateral recess. Interpreted as posterior disk protrusion but cervical laminectomy was negative.

cesses (Fig. 4*B*) resembles disk protrusion into the spinal canal.

Diskography could not be interpreted as entirely normal in any case in our series. In a few instances, a normal nucleus would be encountered at one level but extravasation of contrast medium would be seen at other disk levels. In most cases, disk nuclei were not outlined. The usual finding was one of widespread dissemination of contrast medium throughout the disk, with extension into the lateral recesses, epidural space, or the precervical soft tissues.

During the injection of the contrast medium, all patients had pain, usually in the base of the neck posteriorly, often with radiation into the shoulders, sometimes into the chest, and occasionally down the arms. There was no good correlation of pain radiation with the patient's clinical symptoms or the roentgenographic findings.

Anterior spinal fusion is the procedure most often performed when disk disease is diagnosed by diskography. The disk is removed piecemeal from the anterior side so that it is difficult to recognize disk degeneration or disk protrusion into the epidural space. Hence no good correlation can be obtained between the roentgenographic and the surgical findings. Two of our patients had adequate exploration of the epidural space from the posterior approach by means of laminectomy. No abnormalities of the disks were found despite abnormal appearing diskograms. One of these cases (Fig. 3, *A* and *B*) had widespread extravasation of contrast medium with an appearance suggesting advanced disk degeneration and posterior protrusion.

DISCUSSION

An abnormal cervical diskogram in the absence of significant pathologic findings might be explained in the following ways:

1. It is possible that poor needle placement could account for false extravasation of the contrast medium. This could be the explanation in some cases and at some disk levels; however, needle placement was always checked roentgenographically both in anteroposterior and cross-table lateral views prior to injection without moving the patient. In most instances, the tip of the needle lay close to the center of the disk.
2. Another explanation may be that diskography is a method by which degeneration of the disk due to aging can be demonstrated earlier than possible by plain roentgenograms. This type of disk degeneration more often than not is asymptomatic.[4]
3. Widespread extravasation of contrast medium through the disk might be a normal finding in some patients.
4. What may be called a posterior disk protrusion or herniation by cervical diskography, in some instances, is contrast medium in the lateral recesses projected over the spinal canal in the lateral view (Fig. 4*B*).

Any diagnostic procedure which results in a high proportion of abnormal findings should be open to suspicion. Since cervical disks in our experience generally appeared abnormal by diskography, we feel that caution should be used in interpreting changes as clinically significant.

SUMMARY

Cervical diskography was performed in 32 patients with neck, shoulder, or arm

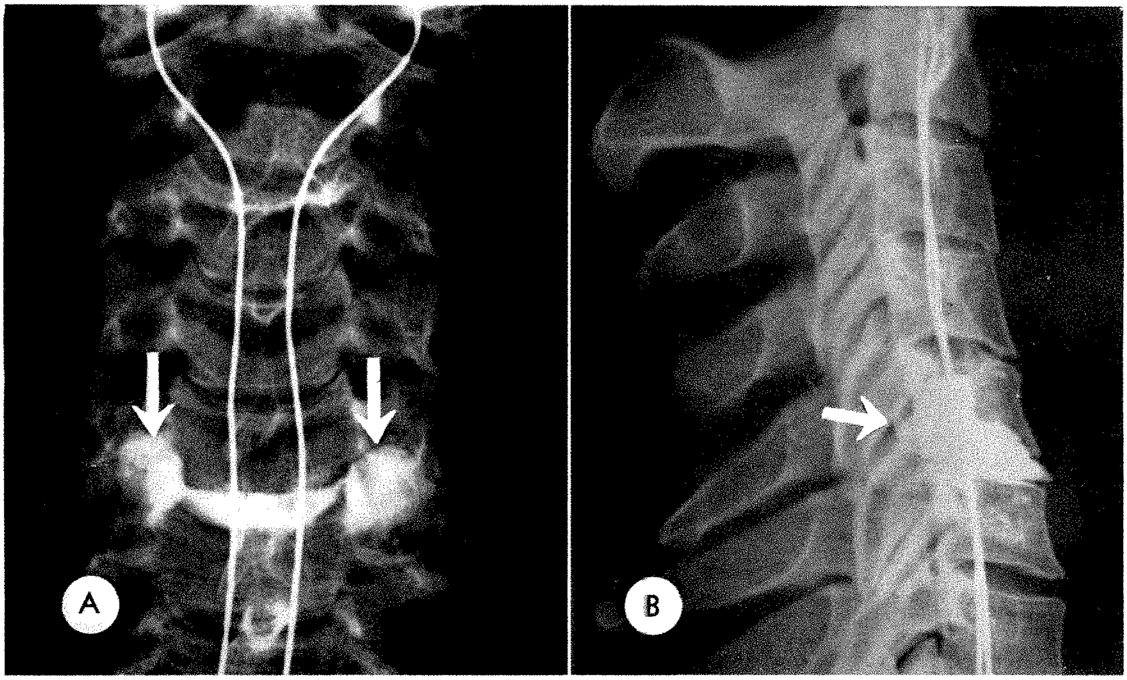


Fig. 4. Roentgenograms of the cervical spine of a skeleton. Cotton was impregnated with hypaque, placed in the intervertebral disk space and lateral recesses but not projecting into spinal canal. (*A* and *B*) Anteroposterior and lateral views show medium in lateral recesses (arrows). Note in *B* that the contrast medium in the lateral recesses projects over spinal canal resembling a posterior disk protrusion.

pain syndromes. The roentgenographic findings were reviewed.

The cervical diskogram was abnormal in every case, the usual picture being widespread extravasation of contrast medium through the disk with extension into the lateral recesses, epidural space, or the precervical soft tissues. Explanations are offered for this phenomenon.

Because of the uncertain status of cervical diskography, caution should be used in interpreting abnormal roentgenographic findings as being of diagnostic significance.

Holy Cross Hospital
1045 East First South Street
Salt Lake City 2, Utah

REFERENCES

1. Cloward, R. B., and Buzaid, L. L. Diskography; technique, indications and evaluation of normal and abnormal intervertebral disk. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1952, *68*, 552–564.
2. Cloward, R. B. Cervical diskography; technique, indications and use in diagnosis of ruptured cervical disks. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1958, *79*, 563–574.
3. Cloward, R. B. Cervical diskography; contribution to etiology and mechanism of neck, shoulder and arm pain. *Ann. Surg.*, 1959, *150*, 1052–1064.
4. Steinert, R. Osteochondrosis of cervical spine. *Radiology*, 1955, *65*, 412–415.
5. Stuck, R. M. Cervical diskography. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1961, *86*, 975–982.

LATERAL INTRATHORACIC MENINGOCELE*

CASE REPORT WITH PREOPERATIVE DIAGNOSIS

By ARTHUR CHANDLER, M.D.,† *and* EUGENE E. HERZBERGER, M.D.‡
MONROE, WISCONSIN

LATERAL intrathoracic meningocele is a rare condition in which there is a protrusion of the dura and arachnoid through a thoracic intervertebral foramen and posterior aspect of the rib cage into the extrapleural thoracic cavity. By itself, the condition is usually asymptomatic, being discovered by roentgenography of the chest as a posterior mediastinal mass density. The first description of this condition was by Pohl[7] in 1933. A review of the subject by Schulte-Brinkmann and Mallinckrodt[9] in 1960 disclosed 41 reported cases, but the number in which a correct preoperative or antemortem diagnosis was made is not indicated. Of 22 cases discussed by Bunner[1] in 1959, a correct roentgen diagnosis was established in only 6.

Despite the rarity of this disorder, there are features which allow the diagnosis to be suspected from clinical evaluation and plain roentgenography of the thorax. Of particular interest and importance is the common occurrence of von Recklinghausen's neurofibromatosis in these patients.

Myelography with gas or iodized oil provides positive diagnosis if a communication between the spinal subarachnoid space and the interior of the meningocele can be demonstrated.

Correct preoperative diagnosis affords appreciation of the neurosurgical aspects of the condition, so that the proper procedure may be planned if surgery seems indicated. In some cases, correct roentgenographic diagnosis makes exploration unnecessary.

The following case illustrates many characteristic features of the condition.

REPORT OF A CASE

The patient, a 68 year old white male retired clerk, was referred by Dr. Melvin Stuessy of Brodhead, Wisconsin, because of weakness of the right upper extremity. He was known to have von Recklinghausen's neurofibromatosis and routine chest roentgenograms had disclosed a right-sided paravertebral mass density which had remained stable since its detection in 1952. He was essentially asymptomatic until about 2 years ago, when he gradually developed weakness in the lower extremities. He did not seek medical attention for this, attributing symptoms to advancing age. Over the past year, he developed progressive weakness and numbness involving the right hand. By September, 1960, he became unable to use this hand and visited his physician, who referred him to our facility on September 9, 1960.

Examination at that time disclosed multiple cutaneous mollusca fibrosa and numerous *cafe au lait* spots. An upper thoracic scoliosis was present. There was severe weakness of the right upper extremity, especially involving the forearm and hand. The interosseous muscles of the right hand were moderately atrophic, and the tendon reflexes of the right arm were exaggerated. Examination of the upper extremities was within normal limits. The lower extremity tendon reflexes were normal; the plantar response on the right was extensor while that on the left was normal.

Roentgenograms of the cervical spine showed narrowing of the intervertebral disk spaces from C4 to C7, with marginal osteophytes at these levels. Oblique projections showed no encroachment on the intervertebral foramina, however. In the thoracic region (Fig. 1), there was a scoliosis convex to the right, with sharp angulation maximal at Th5–Th6. Adjacent to this point, in the right paravertebral region, a soft tissue mass was seen, 4 cm. in greatest dimension. The right fifth posterior intercostal space was widened and there was a suggestion of bone erosion along the right side of the fifth and sixth thoracic vertebrae, although the scoliosis produced such distortion of structures in this region that they were difficult to evaluate. With the history of neurofibromatosis, it was felt that the paravertebral mass could represent either a neurofibroma or a lateral intrathoracic meningocele.

---

* From the Departments of Radiology † and Neurological Surgery ‡ of the Monroe Clinic, Monroe, Wisconsin.

The patient was hospitalized on September 10, 1960, and oil myelography was performed for further evaluation of the neurologic disturbances. Iodized oil was introduced into the lumbar subarachnoid space. No abnormalities were demonstrated in the lumbar or lower thoracic regions. At the site of maximal thoracic angulation oil flowed into the soft tissue mass, between Th5–Th6, and could be readily displaced back into the spinal canal by appropriate positioning of the patient. Thus, the mass was shown to represent a meningocele (Fig. 2). In the cervical region the spinal cord shadow was normal and the root sleeves on the left were normal. On the right there was marked irregularity of the oil column, with retraction at the points of exit of spinal nerve roots from C4 to C7 (Fig. 3). At the conclusion of the study, oil removal was accomplished without difficulty.

In view of the patient's neurologic disturbances, apparently related to the abnormalities seen on the myelogram, it was elected to explore the meningocele. Laminectomy from Th4 to Th7 was performed. The lamina of Th5 indented the dura, and the lamina of Th6 was extremely thin. The dura formed a pouch protruding on the right through an enlarged intervertebral foramen between Th5 and Th6, entering the thoracic cavity through the rib cage at this level. The sac was extrapleural, but was somewhat adherent to the parietal pleura. The dura over the spinal cord was incised at Th5–Th6; the arachnoid at this level was thickened and adherent to the pia and spinal cord. However, the arachnoid lining the meningocele itself appeared normal. No nerve structures entered the sac. The meningocele was withdrawn from the thoracic cavity, its neck ligated and the sac excised. Following mobilization and excision of the sac, the dura over the cord, which before was pulled toward the right and did not pulsate, returned toward the midline and showed normal pulsations. Closure was accomplished in layers, without drainage.

The patient recovered well from the operation. On the day following surgery, he was aware of increased strength in the right hand. He continued to improve at home and has regained good function of the right upper extremity. Some weakness of the legs persists.

Pathologic examination of the excised sac (Dr. Francis C. Tucker) disclosed a fibrous wall, similar to dura. No nerve structures were identified.

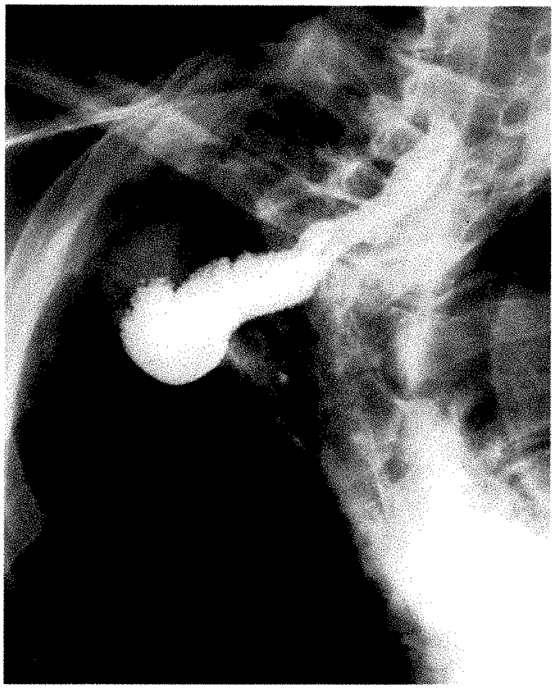


Fig. 2. Oil myelogram demonstrates communication between the subarachnoid space and the upper thoracic paravertebral mass, indicating that the mass represents a meningocele.

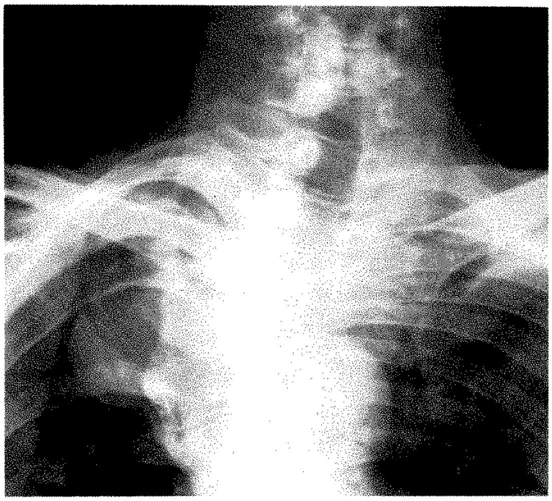


Fig. 1. Plain roentgenogram shows a right paravertebral mass associated with thoracic scoliosis and widening of the fifth posterior rib interspace.

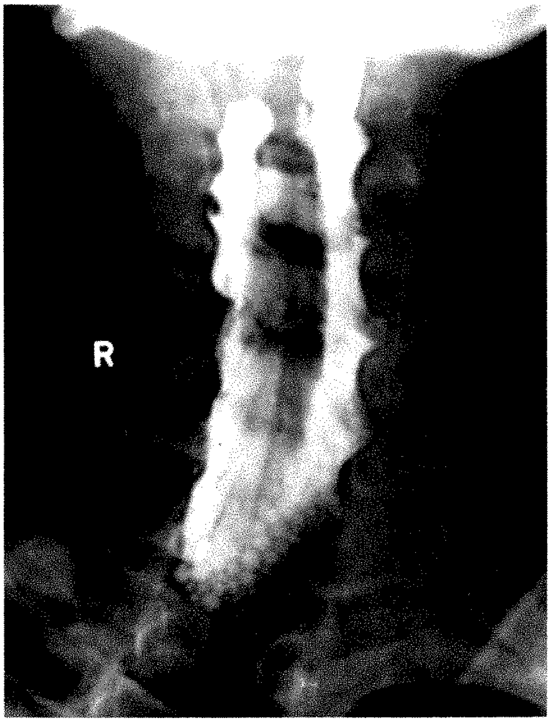


Fig. 3. Cervical area oil myelogram shows the spinal cord shadow displaced to the right, with retraction of the root sleeves along the right side of the oil column.

DISCUSSION

CLINICAL FEATURES

The age range of reported cases has been from 2 days to 63 years, with most discovered in the fourth and fifth decades. The sexes are about equally affected. The condition is usually asymptomatic, but occasionally symptoms may occur, being related to pressure on adjacent structures by the meningocele, or in the present case, to traction upon spinal nerves and meninges as the result of the meningeal herniation. Death has been attributed directly to the meningocele in only one case, where rupture of the sac during coughing was followed by meningitis. In several neonatal deaths, large thoracic meningoceles were present which may have produced respiratory insufficiency.

Von Recklinghausen's neurofibromatosis has been present in three-fourths of reported cases of lateral intrathoracic meningocele. A detailed review of the abnormalities which may be encountered in neurofibromatosis emphasizes that both neuroectodermal and mesodermal dysplasias are basic components of the disease.[5] Whether there is a weakness of the dura or whether local abnormalities of the supporting vertebrae contribute to lateral herniation of the dura is only a matter of speculation.

PATHOLOGY

Most lateral intrathoracic meningoceles occur on the right side. A few have been bilateral and a few have presented on the left. The size is variable; some have nearly filled one hemithorax. The lesion is a lateral out-pouching of the dura and arachnoid through an intervertebral foramen. Associated bony abnormalities in the vicinity of the meningocele are the rule even in the absence of von Recklinghausen's disease.

ROENTGENOGRAPHIC DIAGNOSIS

Plain roentgenograms of the thoracic area reveal a posterolateral mediastinal mass, usually associated with one or more abnormalities of the ribs and thoracic spine. Enlargement of the intervertebral foramen at the site of meningocele is a constant finding; scoliosis with convexity directed toward the meningocele, fused or hypoplastic vertebrae, rib erosion, and erosion of the posterior surface of the vertebral body at the level of the meningocele may be associated. In some instances, laminagrams may show such changes to best advantage.

Lesions characteristic of neurofibromatosis, such as skin nodules and bony dysplasias elsewhere in the thorax may be recognized, giving a clue to the diagnosis.

Myelography provides definite diagnosis by establishing that a communication exists between the meningocele and the spinal subarachnoid space. Gas myelography would be satisfactory, although oil myelography is preferable in cases similar to the one reported in this paper, where information about the spinal cord, nerve roots and subarachnoid space in other regions of the spine is also desired.

The most important differential considerations are neurogenic tumors and neurenteric cysts of the mediastinum, which may simulate lateral meningocele on plain roentgenograms. Similar bone changes may be associated. However, certain authors[1,8] have emphasized that a patient with posterior mediastinal mass and neurofibromatosis is more likely to have an intrathoracic meningocele than an intrathoracic neurofibroma. Myelography readily differentiates these conditions.

TREATMENT

Surgery was performed in 23 of the 41 previously reported cases, with death occurring in 4 instances (meningitis in 2 cases, circulatory collapse in 2). Therefore, if the diagnosis can be established without surgery, operation in asymptomatic cases is not indicated. However, some meningoceles enlarge over a period of years, so that observation is advised. If symptoms occur, related either to pressure on intrathoracic structures or to traction on nerve tissues, surgery is recommended. Surgery should also be considered if observation demonstrates progressive enlargement of the meningocele, or progressive bone erosion. Most cases (without preoperative diagnosis) have been operated upon transpleurally; however, a retropleural approach by laminectomy is generally the most satisfactory.

SUMMARY AND CONCLUSIONS

1. Lateral intrathoracic meningocele is a rare cause of posterolateral mediastinal mass.

2. It is usually asymptomatic, but may be associated with symptoms related to pressure on mediastinal structures or to traction on spinal cord structures.

3. Three-quarters of reported cases have been associated with von Recklinghausen's neurofibromatosis. A posterolateral mediastinal mass in a patient with neurofibromatosis should be suspected of being a lateral meningocele.

4. Diagnosis prior to surgery is important, since surgery may be deferred in asymptomatic cases, and since appreciation of the nature of the mass allows proper planning of the surgical approach in those cases where surgery seems advisable.

5. Surgery is indicated in cases with progressive neurologic disturbances, mediastinal pressure symptoms or enlarging meningocele.

6. A case is reported of a 68 year old man with von Recklinghausen's neurofibromatosis who had neurologic disturbances related to a lateral intrathoracic meningocele. Preoperative diagnosis was established and surgery was successfully performed.

Arthur Chandler, M.D.
The Monroe Clinic
Monroe, Wisconsin

REFERENCES

1. Bunner, R. Lateral intrathoracic meningocele. *Acta radiol.*, 1959, *51*, 1–9.
2. Byron, F. X., Alling, E. E., and Samson, P. C. Intrathoracic meningocele. *J. Thoracic Surg.*, 1949, *18*, 294–303.
3. Ciaglia, P. Intrathoracic meningocele: excision, with three and one-half years follow-up. *J. Thoracic Surg.*, 1952, *23*, 283–296.
4. Goldman, I. R. Congenital malformation of vertebrae (hemivertebrae) with aplasia of corresponding ribs, associated with lateral meningomyelocele: report of case. *A.M.A. Arch. Path.*, 1949, *47*, 153–159.
5. Hunt, J. C., and Pugh, D. G. Skeletal lesions in neurofibromatosis. *Radiology*, 1961, *76*, 1–20.
6. Mendelsohn, H. J., and Kay, E. B. Intrathoracic meningocele. *J. Thoracic Surg.*, 1949, *18*, 124–128.
7. Pohl, R. Mediastinal meningocele simulating round intrathoracic shadow. *Röntgenpraxis*, 1933, *5*, 747–749.
8. Rubin, S., and Stratemeier, E. H. Intrathoracic meningocele; case report. *Radiology*, 1952, *58*, 552–555.
9. Schulte-Brinkmann, W., and Mallinckrodt, H. Spinal changes in Recklinghausen's neurofibromatosis with intrathoracic meningocele. *Bruns' Beitr. klin. Chir.*, 1960, *200*, 257–273.
10. Sengpiel, G. W., Ruzicka, F. F., and Lodmell, E. A. Lateral intrathoracic meningocele. *Radiology*, 1948, *50*, 515–519.

LATE SPINAL BLOCKS AFTER TUBERCULOUS MENINGITIS*

By KAZIMIERZ KOZLOWSKI, M.D.
POZNAN, POLAND

ARACHNOIDITIS from various causes has been reported many times.[1–21] Cases of arachnoiditis were first described in 1898 by Schlesinger and then by Spiller, Musser and Martin in 1903.[6] In 1907, Krause reported that localized arachnoiditis was found six times in a series of 23 patients on whom laminectomies were undertaken for the removal of spinal tumors. In 2 cases, tuberculosis caused narrowing of the spinal canal.[20] Horsley, in 1909, reported that syphilis played a part in the production of meningitis which led to adhesions between the dura, the arachnoid and the cord.[20] Gerstman,[5] in 1915, described 6 cases of chronic circumscribed spinal serous meningitis following gunshot wounds in the region of the spine. Mauss and Krüger[14] reported 14 cases of spinal arachnoiditis, all of traumatic origin. In a series of experimental studies, Harvey[6] demonstrated that arachnoiditis may be induced by pooled blood, serum, homologous tissue, various chemicals and even Ringer's solution. Arachnoiditis following the use of iodized oil was reported by Hurtean *et al.* in 1954.[7] These authors injected pantopaque into the cisterna cerebello-medularis of 12 dogs. After 2 weeks, some of the animals showed a severe cellular reaction in the meninges about the base of the brain, similar to that seen in bacterial meningitis. There are also reports of arachnoiditis following myelography in humans.[7,21] Aseptic, purulent and chronic adhesive meningitis has been reported to occur after spinal anesthesia[10] and after operations on the meninges, spinal cord and the spine.[1,17,18] There have been reports of arachnoiditis following congenital spinal malformations[12] and intervertebral disk disease.[1,4,18] In childhood the principal causes of spinal arachnoiditis are spinal meningitis and tuberculosis of the spinal column.[16]

In the 2 cases here reported, clinical signs of cauda equina involvement developed 7 and 9 years, respectively, after tuberculous meningitis. Spinal adhesive arachnoiditis was diagnosed in both cases. Similar cases were not found in the available literature.

REPORT OF CASES

CASE I. K.P. (No. 226-60), a male born on June 20, 1950, was admitted to the I Pediatric Clinic in Poznan, Poland, on March 23, 1960. He complained of low back pain of about 1½ years' duration. The pain appeared upon arising from bed in the morning, after a long period of lying, after sneezing, coughing or forward flexion, and after a short period of sitting at the table.

When he was 3 years old, he was hospitalized for 8 months because of tuberculous meningitis. He was treated with streptomycin, intramuscularly and intrathecally. During his stay in the hospital, a total of 51 lumbar punctures was performed, 39 of which were made for the administration of 1,480 mg. of streptomycin intrathecally. He was discharged in good condition. There was no relapse of the disease. When the low back pain occurred, he was treated with analgesic drugs and diathermy, but showed no improvement.

At the time of admission, his general state was good. He weighed 29.3 kg. The physical examination showed normal findings in the chest and abdomen. The neurologic examination disclosed flattening of the lumbar lordosis. The sacral region was painful to percussion. The maximal forward flexion when standing was 25–30°. He was unable to bend further because of pain in the sacral region. Limitation of back flexion was also noted. He could not sit with straightened legs. The sciatic stretch test was positive at 35°. Pain and temperature sensations and superficial sensation were normal. The skin and tendon jerks were within physiologic limits. He walked with a step gait. Laboratory findings revealed normal blood and urine. The lumbar puncture revealed a positive Pandy test, protein 158 mg. per cent, cells 2/mm.^{3}, sugar 62 mg. per cent, and a slightly lowered spinal fluid pressure. Suboccipital puncture showed a negative Pandy test, protein 55 mg. per cent, cells 2/mm.^{3}, and sugar 55 mg. per cent. The eye grounds were normal. The roentgen appearance of the skull and vertebral column was normal. Myelograms demonstrated a complete block at the L4-L5 level, with the contrast material appearing as a half-oval, regular filling defect (Fig. 1, *A* and *B*). In roentgenograms taken 12 days later, the residual contrast substance was noted partly below the obstruction and presented as an oval filling defect with somewhat irregular borders between L4 and L5. The upper margin was oval; the lower, horizontal (Fig. 2). The appearance of the first myelogram suggested an intradural neoplasm, but a careful examination of the roentgenograms taken 12 days later indicated arachnoiditis.

---

* From the I Pediatric Clinic of the Medical School of Poznan, Poland. Director: Prof. Dr. Med. T. Rafinski.

Varidase was injected intrathecally on two occasions, 3,000 and 2,000 units, respectively. After each puncture the patient vomited, complained of a headache and showed a temperature rise to 39°C. Meningeal signs appeared. The cerebrospinal fluid showed an inflammatory reaction. After $2\frac{1}{2}$ months in the hospital, he was allowed to go home with a recommendation for subsequent physical therapy.

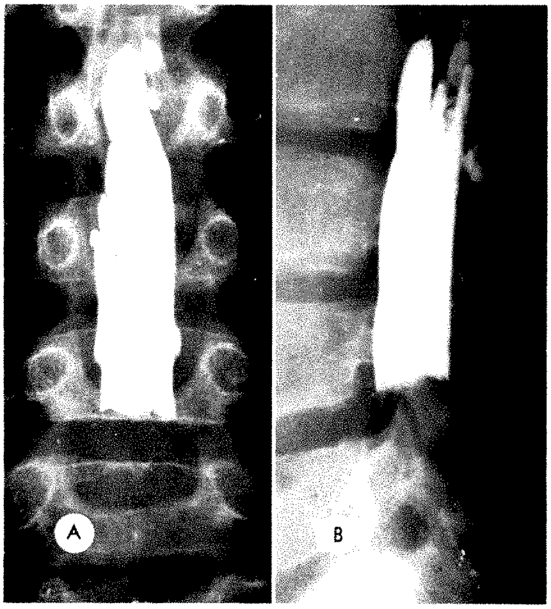


FIG. 1. Case I. (*A*) Posteroanterior and (*B*) lateral myelograms show complete block at L4-L5 level.

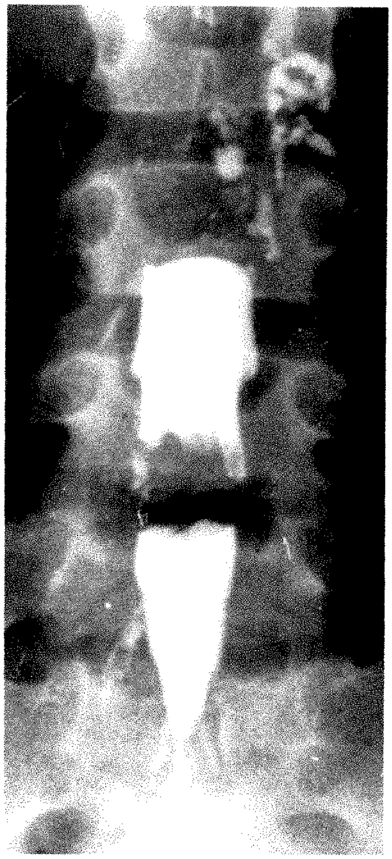


FIG. 2. Case I. Roentgenogram made 12 days after Figure 1 shows the residual contrast medium past the obstruction which now presents as a filling defect in the column.

CASE II. K.A. (No. 531-60), a male born on December 18, 1950 was admitted to the I Pediatric Clinic in Poznan, Poland, on July 9, 1960. He complained of low back pain on forward flexion, sneezing, coughing and jumping. The parents thought that his complaints were due to trauma he suffered in the sacral region in June, 1958. In subsequent months, the pain increased and an orthopedic surgeon was consulted, who excluded the possibility of bone disease. A psychiatric examination was normal. After a neurologic examination, the parents were told that an irritation of the lumbosacral nerve roots was present. Some analgesic drugs were prescribed but the patient showed no improvement. Another orthopedic surgeon was

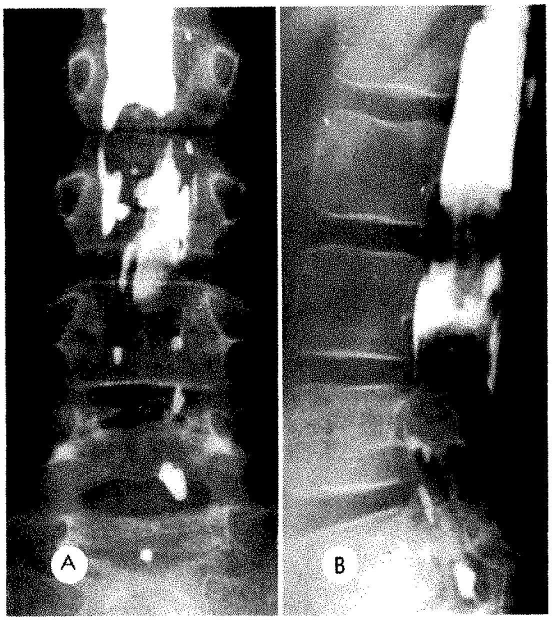


Fig. 3. Case II. (*A*) Posteroanterior and (*B*) lateral myelograms show a partial block at the L2 and L3 level with several discrete filling defects. Compare with Figure 2.

consulted who made a diagnosis of right sided sacroiliac tuberculosis. The child was sent to a sanatorium, where after 6 weeks tuberculosis was eliminated as a possibility and a diagnosis of right sacroiliac arthrosis was made.

At the age of 6 months, the patient had been hospitalized for a 6 month period because of tuberculous meningitis. He received streptomycin intramuscularly and intrathecally. During his stay in the hospital, a total of 55 lumbar punctures were performed, 45 of which were made for the administration of 1,240 mg. of streptomycin intrathecally. He was discharged in good health. No spinal block was noted during his stay in the hospital and there was no relapse of the disease.

At the time of admission to the clinic, his general state was good. He weighed 24.6 kg. The physical examination showed normal findings in the chest and abdomen. The neurologic examination revealed flattening of the normal lumbar curve. The sacral region was painful to percussion. The maximal forward flexion at standing was 20°. He could not bend further because of pain in the sacral region. There was also limitation of back flexion. The sciatic stretch test was positive at 30°. Pain and temperature sensations and superficial sensation were normal. The skin and tendon jerks were normal. Laboratory findings revealed normal blood and urine. Lumbar puncture showed a positive Pandy test, protein 84 mg. per cent, cells 9/mm.^{3}, some erythrocytes, sugar 55 mg. per cent, and a decreased spinal fluid pressure. The eye grounds were normal. The roentgen appearance of the skull and vertebral column was normal. The sacroiliac joint space on the right upper side was not clear. In its medial portion a linear shadow was noted which was originally thought to correspond to a sclerotic shell around an osteolytic process, although some consideration was given to its being the result of superimposition of the sacral and iliac bones. Special studies of the right sacroiliac joint revealed no abnormalities. On myelograms a partial block was noted at the level of L2, with the contrast medium appearing as a smooth half-oval filling defect. Some of the opaque material flowed down, and a second partial block was visualized at the level of L3 with the contrast material again presenting as a half-oval filling defect. Some opaque material was noted below this point in the form of streaks (Fig. 3, *A* and *B*). The contrast medium was partially removed. On roentgenograms made 24 hours later, the contrast material appeared as two oval filling defects. Some of the contrast substance flowed downward and formed streaks and droplets (Fig. 4, *A* and *B*). The remainder filled the end of the dural sac. The roentgen diagnosis was arachnoiditis.

Varidase was injected intrathecally on two occasions, 3,000 and 2,000 units, respectively. After each puncture the patient vomited, complained of a headache and the temperature rose to 39°C. Meningeal signs appeared. The cerebrospinal fluid showed an inflammatory reaction. After 2 months in the hospital, he was discharged home without improvement and with recommendation for physical therapy.

DISCUSSION

The gelatinous exudate in tuberculous meningitis is present at the base of the brain and at the sylvian fissure. Some exudate may be present over the convexity of the brain. The spinal cord is edematous and the meninges of the cord show some exudate throughout their course.[2] As a result of this congestion of the meninges and of the tuberculous exudate, it is reasonable to suppose that spinal obstruction can be produced readily (Table 1).

Spinal blocks are not rare in cases of tuberculous meningitis. They may appear in the acute stage of the disease (early blocks), or later, in the chronic stage (late blocks). Early spinal obstructions may be found even at the beginning of treatment, in cases in which a late diagnosis has been made. The late spinal blocks appear between the second and sixth month of treatment, usually in the third and fourth months.[11]

The spinal blocks may be recognized by changes in the cerebrospinal fluid such as increased protein content, a decreased number of white blood cells, xanthochromia, pathologic Queckenstedt phenomenon, or the Froin syndrome; and clinically by hyperesthesia, spastic or flaccid paresis and disturbances of sphincter control.

Many reports have appeared on spinal blocks in cases of tuberculous meningitis.[9,11,13,19,22] Some authors believe that the spinal obstructions may be the result of two different factors: (1) tuberculous arachnoiditis, and (2) reactive arachnoiditis after intrathecal sterptomycin injections. In the second group, the streptomycin irritates the meninges already damaged by the tuberculous disease and only precipitates the block. This explanation is supported by the fact that spinal obstruction may be found before any treatment is started as well as in cases of pulmonary tuberculosis which have been treated with streptomycin intramusculary. Spinal blocks are not found in patients treated with streptomycin for reasons other than tuberculosis. Moreover, the most usual site for spinal blocks is in the thoracic part of the vertebral column.[8]

Others feel that the spinal blocks are the result of streptomycin injected intrathecally in doses that are too great or in too concentrated a form. The majority of spinal blocks appear in the second month of treatment with signs of nerve root irritation. They subside when the intrathecal punctures of streptomycin are stopped. No anatomicopathologic changes in the spinal region were noted in cases which were not treated or which were treated very briefly with streptomycin.[9,11,13] It may be possible that frequent lumbar punctures alone can cause mechanical arachnoiditis.

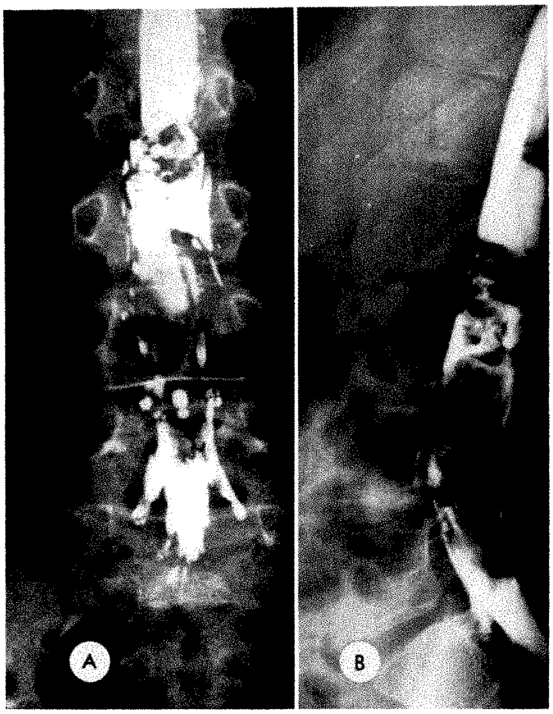


FIG. 4. Case II. (*A* and *B*) Roentgenograms made 24 hours after Figure 3. The 2 filling defects at the L2 and the L3 to L4 levels are clearly shown. The streaks and droplets suggest adhesive arachnoiditis rather than tumor.

It is probable that the principal cause of the spinal obstruction in tuberculous meningitis is the tuberculous process, but that streptomycin plays a role in intensifying the proliferative reaction, especially in cases treated for too long a period or with excessive doses. The degree of concentration may also play a part in the production of the spinal blocks.

The course of arachnoiditis from any cause may be very slow and a number of years may elapse before the patient seeks advice. A prominent feature of the disease is pain in one or both legs. Paresthesias, spasticity and weakness appear. Objective loss of sensibility eventually develops. The tendon reflexes are increased and the plantar reflexes are of the extensor type. Disturbances of sphincter control develop late in the course of the disease. The picture may be identical with that of a slowly growing extramedullary neoplasm.[3]

It is generally believed that partial and even total spinal blocks do not produce any symptoms if the spinal cord is not damaged. The only serious complication is a relapse of the disease due to incompletely healed miliary foci in the meninges. The pathodynamics of the healing tuberculosis exudate under the influence of streptomycin in the meninges and in the visceral miliary lesions consist of diminishing cellularity and progressive fibroplasia.[9,11,13,19,22]

The discontinuance of intrathecal injections of streptomycin, as a consequence of the introduction of new antituberculous drugs and adrenal hormones, should result in a decreased number of spinal obstructions in patients with tuberculous meningitis. Majewska[13] claims that no blocks were observed in cases which were treated early and without streptomycin. Kaminska and Kulczynska[9] did not notice any diminution of the frequency of spinal blocks since they began using the new antituberculous drugs and discontinued intrathecal streptomycin injections; however, the character of the blocks has changed. Total and late spinal blocks were no longer observed and the duration of the blocks was shortened. These conflicting observations may be explained by the different material studied. Majewska worked with adults and the treatment in her cases was probably started early. The cases of Kaminska and Kulczynska were children and in many the disease was not recognized in the early stage.

In both of our cases, no spinal obstruction was noted during the course of the disease. Both children left the hospital without any residuals of the disease and with normal cerebrospinal fluid. For a period of 7 and 9 years, respectively, the children were well and had no further complaints.

It is impossible to decide whether the cause of the arachnoiditis in our cases was tuberculous meningitis, intrathecal injec-

TABLE I

INCIDENCE OF SPINAL BLOCKS FOUND WHILE TREATING TUBERCULOUS MENINGITIS

Authors	No. of Cases	No. of Spinal Blocks	Per Cent of Spinal Blocks	Complete Recovery	Recovery with Some Residuals	Deaths	Remarks
Zych *et al.*[22] 1948–1956	126 (adults)	38	30.1	14	7	17	
Kepinski and Kropaczek[11] 1949–1953	148 (adults)	40	27.2	22		18	
Sommer[19] 1948–1851	26 (children and adults)	11	42.3			12	
Kaminska and Kulczynska[9] 1946–1959	639 (children)	44	7	30		14	Early blocks 16 Late blocks 28 Partial blocks 39 Total blocks 5
Majewska[13] 1949–1953	115 (adults)	11	9.5	9		2	

tions of streptomycin, mechanical trauma from lumbar punctures, or a combination of these.

In Case I, the clinical symptoms appeared 7 years after tuberculous meningitis, and increased very slowly. In Case II the first symptoms were noted after trauma. Quite often chronic disease of the spinal region in children is discovered after a slight accident. An anatomic variant in the right sacroiliac joint resulted in a diagnosis of tuberculosis. The clinical symptoms were similar in both cases and these had not progressed during the previous 1½ years in either. One may anticipate, however, an intensification of symptoms during the rapid growth period in adolescence.

The late clinical appearance of the arachnoiditis may be explained in 2 ways: (1) the inflammatory process in the meninges could advance after the clinical healing of the disease; and (2) the so-called ascent of the spinal cord which occurs with the growth of a child causes stretching of the adhesions and compression of the nerves of the cauda equina. In the newborn, the blunt end of the medullary conus ends at the level of L3, and in an adult may lie between L1 and L2.[16]

The fibrolytic enzymes cannot be of any help at this stage of the disease. We do not feel that surgery is indicated in these cases since an operation for adhesions in the cauda equina region is difficult to perform and very often the symptoms appear to increase after surgical intervention. We believe that physical therapy is the treatment of choice at the present time.

In the differential diagnosis, spinal neoplasms must be taken into consideration. It may be very difficult to establish the correct diagnosis, as the history, the neurologic examination, and the myelographic findings may be identical in both conditions. Although this was true in our cases, there was, in addition, a history of tuberculous meningitis in each. Loss of sensibility, muscular atrophy, asymmetry or absence of skin or tendon reflexes were not noted. The partial blocks in both cases were situated at the level where lumbar punctures were performed. There had been no progress of the disease during the previous 1½ years. These factors aided us in making the diagnosis of chronic spinal arachnoiditis.

SUMMARY

Two cases of spinal arachnoiditis in children in whom symptoms appeared clinically 7 and 9 years, respectively, after tuberculous meningitis have been described. No similar cases have been found in the literature. The pathogenesis of spinal blocks in tuberculous meningitis has been discussed and the influence of the tuberculous process, the streptomycin therapy, and the lumbar punctures as possible etiologic factors is stressed. The late appearance of the clinical symptoms in these cases seems to be the result of the so-called ascent of the spinal cord, with adhesions causing secondary stretching of the spinal roots of the cauda equina.

K. Kozlowski, M.D.
UL. Roosevelta 9M1
Poznan, Poland

The author expresses his appreciation to Dr. F. N. Silverman for reviewing this paper.

REFERENCES

1. Davidoff, L. M., Gass, H., and Grossman, J. Postoperative spinal adhesive arachnoiditis and recurrent spinal cord tumor. *J. Neurosurg.*, 1947, *4*, 451–464.
2. Dietrich, A. Allgemeine Pathologie und Pathologische Anatomie. Vol. III. Fifth edition. Edited by Hirzel, 1939, pp. 336–337.
3. Ford, F. Acquired diseases of spinal cord. In: Brennemann's Practice of Pediatrics. Vol. IV. Edited by Prior Company, Hagerstown, Maryland, 1960, pp. 25–28.
4. French, J. D. Clinical manifestations of lumbar spinal arachnoiditis: report of thirteen cases. *Surgery*, 1946, *20*, 718–729.
5. Gerstman, J. Beiträge zur Pathologie des Rückenmarks zur Frage der Meningitis serosa und sero-fibrinosa circumscripta spinalis. *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1915, *29*, 97–167.
6. Hassin, G. B., and Andrews, E. Serous spinal meningitis (circumscribed): report of 2 cases. *J.A.M.A.*, 1929, *92*, 877–880. Citing: Schlesinger, H. Beiträge zur Klinik der Rücken-

marks- und Wirbeltumoren. Jena. Fischer Verl., 1898, pp. 46, 162, 163; Spiller, W. G., Musser, J. H., and Martin, E. Case of intradural spinal cysts with operative recovery. *Univ. Pennsylvania M. Bull.*, 1903, *16*, 27; and Harvey, S. C. Meningeal adhesions and their significance. *Inter-State Post. Grad. M. A., North America Proc.*, 1926, *27*, 2.

7. Hurtean, E. F., Baird, W. C., and Sinclair, E. Arachnoiditis following use of iodized oil. *J. Bone & Joint Surg.*, 1954, *36A*, 393–400.
8. Janbon, M., Bertrand, L., and Salvaing, J. Sur la fréquence réelle des arachnoidites spinales dans la tuberculose méningée. *Semaine hôp.* Paris, 1951, *27*, 363–364.
9. Kaminska, M., and Kulczynska, K. Niedroznosc kanalu kregowego w gruzliczym zapaleniu opon mozgowo-rdzeniowych i mozgu. To be published.
10. Kennedy, F., Effron, A. S., and Perry, G. Grave spinal cord paralyses caused by spinal anesthesia. *Surg., Gynec. & Obst.*, 1950, *91*, 385–398.
11. Kepinski, A., and Kropaczek, Z. Wodoglowie i niedroznosc kanalu rdzeniowego w przebiegu gruzliczego zapalenia mozgu i opon mozgowo-rdzeniowych u doroslych. *Gruzlica*, 1954, *22*, 771–786.
12. Lindgren, E. Myelographic changes in kyphosis dorsalis juvenilis. *Acta radiol.*, 1941, *22*, 461–470.
13. Majewska, Z. Blok rdzeniowy w przebiegu gruzliczego zapalenia opon mozgowo-rdzeniowych. *Neurol. Neurochir. Psychiatr. Polska*, 1955, *4*, 533–561.
14. Mauss, T., and Krüger, H. Über die unter der Meningitis serosa circumscripta verlaufenden Kriegsschädigungen des Rückenmarkes und ihre operative Behandlung. *Deutsche Ztschr. f. Nervenh.*, 1918, *62*, 1–116.
15. Pansini, K., Skrivaneli, N., and Spidla, M. La méningite tuberculeuse spinale isolée. *Arch. franç. pediat.*, 1955, *12*, 542–546.
16. Rozycki, S. Anatomia mozgowia i rdzenia kregowego. Edited by Ksiegarnia Akademicka Poznan, 1947, pp. 182–183.
17. Seaman, W. B., Marder, S. N., and Rosenbaum, H. E. Myelographic appearance of adhesive spinal arachnoiditis. *J. Neurosurg.*, 1953, *10*, 145–153.
18. Smolik, E. A., and Nash, F. P. Lumbar spinal arachnoiditis; complication of intervertebral disc operation. *Ann. Surg.*, 1951, *133*, 490–495.
19. Sommer, A. R. Tuberculous meningitis: some aspects of its treatment. *Brit. M. J.*, 1952, *47*, 356–360.
20. Walshe, F. M. R. Serous spinal meningitis. *M. Sc. Abstr. & Rev.*, 1919–1920, *1*, 318–323. Citing: Krause, Zur Kenntniss der Rückenmarklähmungen. *Neurol. Centralbl.*, 1907, *26*, 383; and Horsley, V. On chronic spinal meningitis. *Brit. M. J.*, 1909, *1*, 513.
21. Wellauer, J. Die Myelographie mit positiven Kontrastmitteln. Georg Thieme Verlag, Stuttgart, 1961.
22. Zych, D., Krysinski, J., Kwiekowa, A., and Zajaczkowska, J. Wyniki leczenia gruzliczego zapalenia opon mozgowo-rdzeniowych u dorosłych bez dokanałowego stosowania leków przeciw pratkowych oraz wartosc kortikoterapii. *Gruzlica*, 1957, *25*, 277–286.

SPINAL EXTRADURAL CYSTS*

WITH REPORT OF AN OSSIFIED SPINAL EXTRADURAL CYST

By DAVID J. ROSENBLUM, M.D., *and* JOSHUA R. DEROW, M.D.
BROOKLYN, NEW YORK

SPINAL extradural cysts may be the cause of long standing or persistent neurologic symptoms. Their insidious evolution is illustrated by our Case I in which the cyst was present long enough for the wall to ossify. To our knowledge this is the first such case to be recorded.

REPORT OF CASES

CASE I. N.R., a 49 year old white female, underwent laminectomy for a herniated disk 22 years ago. She did well postoperatively but had intermittent foot drop and pain. Five months prior to admission the patient had an exacerbation of her pain and neurologic findings. Physical examination revealed decreased pain and temperature sensation along the lateral aspects of the foot and lower leg.

Roentgenograms (Fig. 1) demonstrated an oval area of calcification in the area of the previous laminectomy. A spinal fusion had not been performed.

Surgery revealed a spinal extradural cyst extending from the lower border of the third lumbar vertebra to the fourth sacral vertebra. It contained spinal fluid and had a thin membranous wall containing bone and calcium. After removal of the cystic area, a communication with the subdural space measuring 1 × 1 cm. was found at the site of the previous disk. A second small opening several millimeters in size was noted. There was no gross abnormality of the cauda equina. A herniated disk was not present.

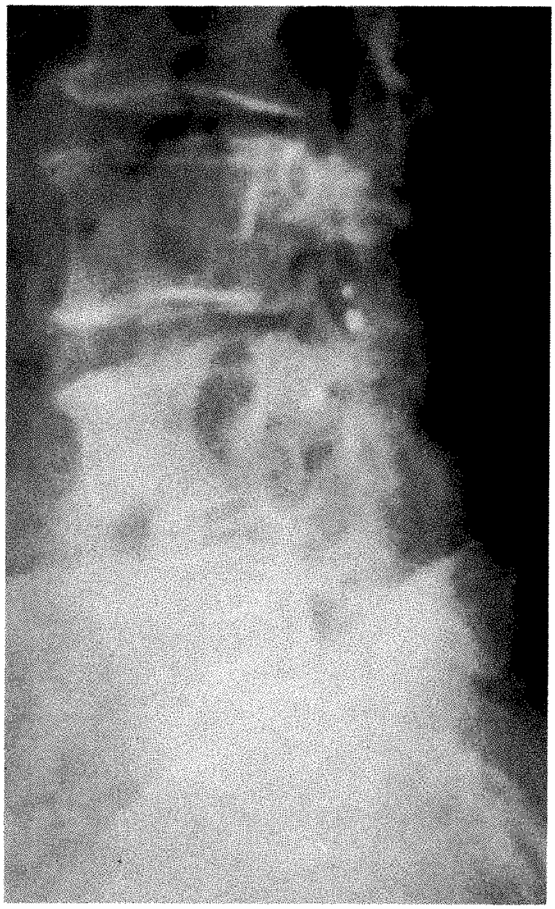


FIG. 1. Case I. An oval area of calcification is seen extending from the lower border of L-3 over the sacral area.

CASE II. J.W., a 45 year old white male construction worker, gave a history of a fall from a 16 foot ladder 2 years prior to his admission. He returned to work after several days and was asymptomatic until 1 year previously when he had an onset of low and midback pain with radiation to the left anterior thigh and inguinal regions. This pain became progressively worse and finally there was a feeling of numbness and tingling of the left lower extremity. There was no motor deficit.

Physical examination revealed a sensory deficit on the left up to and including T-12 and on the right up to and including L-1. Lower extremity reflexes were generally hyperactive; both plantar reflexes were flexor.

Roentgenograms (Fig. 2, *A*, *B* and *C*) revealed destruction of the left pedicles of T-12 and L-1 and a concave indentation of the posterior surface of the body of L-1 with the edge of the bone well eburnated, indicating pressure erosion. Laminagrams demonstrated widening of the interpediculate spaces at T-12 and L-1 and thinning of these pedicles on the left side.

---

* From the Departments of Radiology of Long Island College Hospital, The Brooklyn Veterans Administration and The State University of New York, Downstate Medical Center.

A myelogram (Fig. 3) showed a slowing of the flow of the opaque column at L-1 and a marked

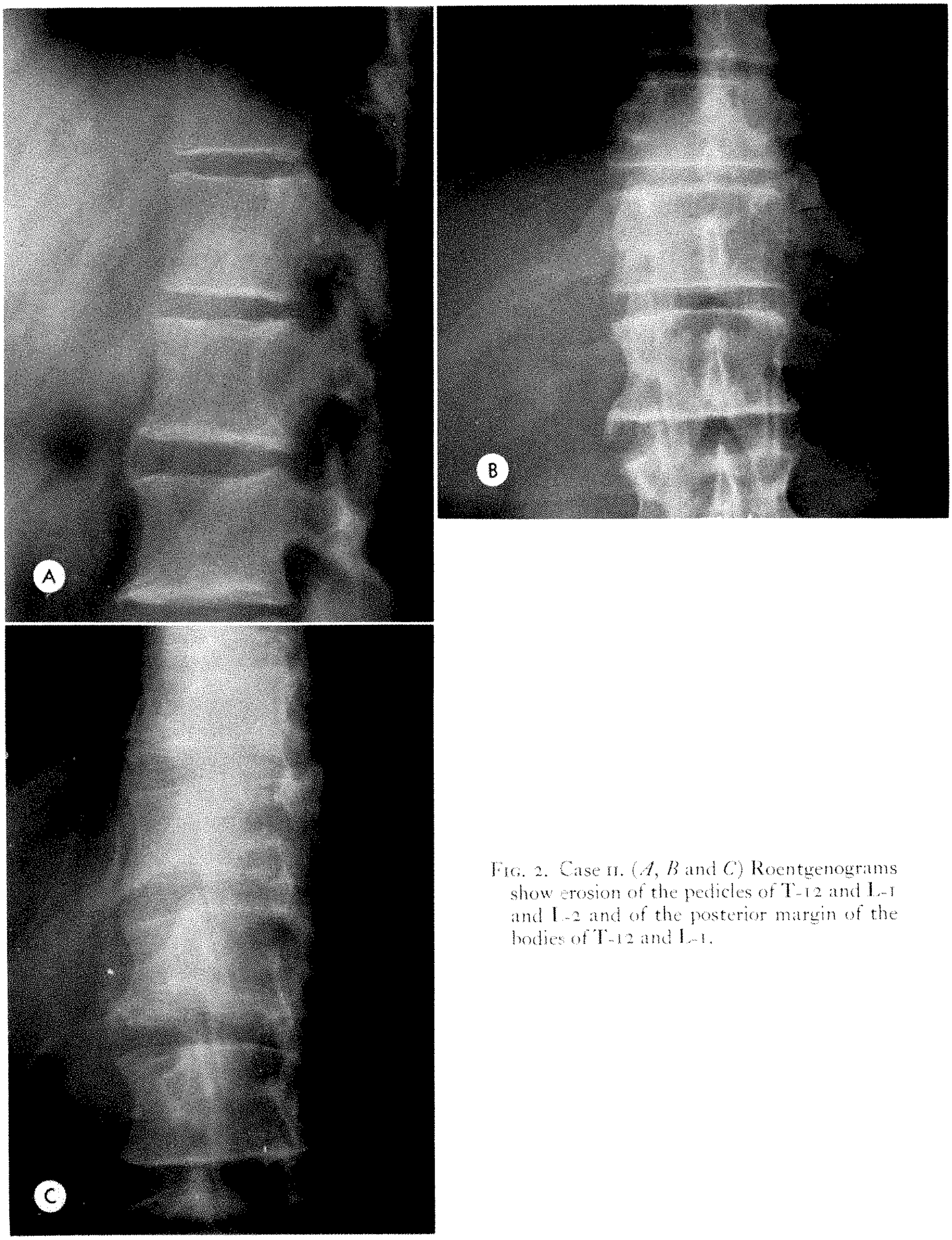


Fig. 2. Case II. (*A*, *B* and *C*) Roentgenograms show erosion of the pedicles of T-12 and L-1 and L-2 and of the posterior margin of the bodies of T-12 and L-1.

displacement of the opaque column to the right by a spindle-shaped mass.

Surgery disclosed a large extradural cyst containing cerebrospinal fluid at the level of T-12 and L-1 with marked displacement of the normal dura to the right. The cyst was present ventral to the dural sac and had eroded the bodies of T-12 and L-1. At the cephalic border of the cyst there was a 0.7 cm. rent through which protruded a large bubble of arachnoid which drained cerebrospinal fluid into the cavity. The appearance was that of a leptomeningeal extradural cyst.

DISCUSSION

Extradural cysts are of two types, congenital and acquired. The congenital variety is usually found in the midthoracic area and is associated with bony changes such as a wide spinal canal due to erosion and a mild scoliosis or kyphosis juvenilis. It is most commonly found in adolescents. The congenital variety has also been reported in the cervical region and dorsolumbar region without osseous changes. Cloward and Bucy[1] believed the kyphosis to be due to impaired venous drainage of the vertebral bodies.

There are two major theories as to the development. Some investigators[2] believe that the cyst is lined with arachnoid and caused by herniation of arachnoid through a congenital defect in the dura or a diverticulum of the dura. Others[5] feel that the congenital cyst arises from misplaced or detached rests of cells. From the surgical and histologic descriptions it seems possible that both theories may be correct.

The acquired type may develop following trauma, intramural hemorrhage, or surgery. Root sleeve damage may occur when removing a lateral disk. An extradural cyst may also form following excision of a tumor especially when part of the dura has been sacrificed as in removing the base of a meningioma or deliberately leaving the dura open as in removal of a spinal epidural malignancy.

The acquired type may have an arachnoid lining or may be a spurious meningocele with a fibrous tissue wall.[7] The former forms when the arachnoid herniates through a defect in the dura, and the latter is formed when a chronic communication between the arachnoid and paravertebral region exists. The cerebrospinal fluid sets up a connective tissue reaction, with formation of a pseudocystic cavity. Case I is the first reported case where the wall showed evidence of calcification and ossification. Bony changes may be produced by the acquired type as in Case II. Both types may or may not be entered by opaque media.[4,8]

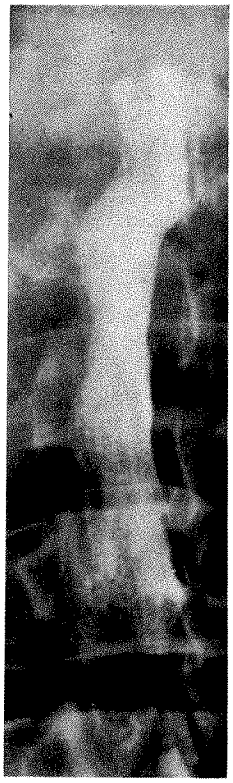


Fig. 3. Case II. A myelogram shows extradural pressure on the pantopaque column.

Cysts of both types may be present for varying lengths of time before producing symptoms. Those in the lumbar area are more apt to be present a longer period of time because the cauda equina can withstand compression better than the cord, and the canal is slightly wider. Case II presented symptoms a short time following trauma, and bone erosion was seen on the roentgenogram. Another factor which will affect onset of symptoms is the size of the communication with the subarachnoid space. Where fluid flows freely between the cyst and the subarachnoid space, symptoms will usually have a later onset. The associated bony changes depend on the location and the patient's age when the cyst is formed.

SUMMARY

Spinal extradural cysts may be congenital or acquired. A case of a spinal extradural cyst which was present long enough for the wall to ossify and calcify is reported. They may be very slow in forming, and it is important to consider an extradural cyst when there are recurrent symptoms following surgery.

David J. Rosenblum, M.D.
340 Henry Street
Brooklyn 1, New York

We would like to thank Dr. E. J. Browder, Professor Emeritus of Neurosurgery of the State University of New York Downstate Medical Center, for permission to use Case 1.

REFERENCES

1. Cloward, R. B., and Bucy, P. C. Spinal extradural cyst and kyphosis dorsalis juvenilis. Am. J. Roentgenol. & Rad. Therapy, 1937, *38*, 681–706.
2. DuToit, J. G., and Fainsinger, M. H. Spinal extradural cysts. *J. Bone & Joint Surg.*, 1948, *30B*, 613–618.
3. Elsberg, C. A., Dyke, C. G., and Brewer, E. D. Symptoms and diagnosis of extradural cysts. *Bull. Neurol. Inst. New York*, 1934, *3*, 395–417.
4. Good, C. A., Adson, A. W., and Abbott, K. H. Spinal extradural cyst (diverticulum of spinal arachnoid): report of case. Am. J. Roentgenol. & Rad. Therapy, 1944, *52*, 53–56.
5. Hyndman, O. R., and Gerber, W. F. Spinal extradural cysts, congenital and acquired: report of cases. *J. Neurosurg.*, 1946, *3*, 474–486.
6. Mayfield, F. H., and Grantham, E. G. Spinal extradural cysts. *Surgery*, 1942, *11*, 589–595.
7. Pagni, C. A., Cassinari, V., and Bernasconi, V. Meningocele spurius following hemilaminectomy in case of lumbar discal hernia. *J. Neurosurg.*, 1961, *18*, 709–710.
8. Schreiber, F., and Haddad, B. Lumbar and sacral cysts causing pain. *J. Neurosurg.*, 1951, *8*, 504–509.
9. Swanson, H. S., and Fincher, E. F. Extradural arachnoidal cysts of traumatic origin. *J. Neurosurg.*, 1947, *4*, 530–538.
10. Turner, O. A. Spinal extradural cyst: report of case with particular reference to possible diagnostic aid. *A.M.A. Arch. Neurol. & Psychiat.*, 1947, *58*, 593–600.

VOL. 90. No. 6

DISPLACEMENT OF THE LINEAR THORACIC PARASPINAL SHADOW OF BRAILSFORD

AN EARLY SIGN IN OSTEOMYELITIS OF THE THORACIC SPINE

By D. GLYN MILLARD, M.B., B.S. (Lond.)*
BOSTON, MASSACHUSETTS

> *Something hidden. Go and find it. Go*
> *and look behind the Ranges – – – – –*
> *Something lost behind the Ranges.*
> *Lost and waiting for you. Go!*
> Rudyard Kipling.

THE *linear thoracic paraspinal shadow* is a slender vertical line of demarcation often seen on an anteroposterior roentgenogram of the thoracic spine. It is usually on the left, but it is seen, though less frequently, on the right side as well. It extends from T4 to the reflection of the pleura on to the diaphragm and is medial to the descending aorta which, being more opaque than the lung, will also be seen as a linear shadow.[1]

In 1943, prompted by an editorial a year earlier,[3] Brailsford[1] explained and reported that this linear thoracic paraspinal shadow represented the posteromedial border of the lung in apposition to the mediastinal pleura. Although this shadow was frequently an enigma,[3] Brailsford stated that it was of great importance in the diagnosis of lesions involving the thoracic spine.

The early diagnosis of pyogenic osteomyelitis of the vertebrae, a painful and crippling condition, is difficult because of its protean manifestations.[10] The known roentgenographic changes of bone destruction of the vertebral bodies with associated involvement of the intervertebral disk, the proliferative periosteal reaction, and the accompanying soft tissue mass[8,9,10] are present when the disease is well under way and is chronic. A review of the radiologic literature fails to reveal any mention of the lateral displacement of the linear thoracic paraspinal shadow on a chest roentgenogram as an aid in the early diagnosis of osteomyelitis of the thoracic spine.

It is proposed to discuss a case of pyogenic osteomyelitis of the thoracic spine in a 17 year old male, with sequential roentgenograms of the chest illustrating this displacement away from the midline, an early sign of thoracic spine involvement, and the later development of the classic late signs.

ROENTGENOLOGIC MANIFESTATIONS OF THE MEDIASTINUM

The initial sites of pyogenic infection of the thoracic spine may be the vertebral arches, transverse processes, or the periphery of the vertebral bodies. The center of the body is not usually involved.[8,9,10] The accumulation of edema and inflammatory exudate in the paravertebral region would cause lateral displacement of the linear thoracic paraspinal shadow which can be detected, on the left, through the aortic shadow on the chest roentgenogram because there is a soft tissue-air surface to produce contrast. This displacement, which is small, is difficult to detect on the right because there is no opaque structure, such as the aorta, to act as a measuring stick.

The initial soft tissue response would consequently be in the posterior mediastinum where the search should begin to detect displacement of the linear thoracic paraspinal shadow.

The roentgenographic interpretations are presented in Table I. Figure 1 demonstrates the linear displacement of the left mediastinal pleura and the gradual appearance of a right paravertebral globular mass. Figure 2 shows the roentgenographic manifestations of the bone changes produced by a pyogenic infection of the thoracic spine.

---

* Radiologist, Monadnock Community Hospital, Peterborough, New Hampshire; Clinical Assistant in Radiology, Massachusetts General Hospital, Boston, Massachusetts.

There is destruction of the inferior aspect of T7 on the left and partial destruction of the superior aspect of T8. There is a small amount of calcification in the soft tissue just to the left of the inferior portion of T7. This is more obvious on the postoperative roentgenogram of December 28, 1960. Roentgenograms made on June 19, 1961, and September 13, 1961, show gradual healing and diminution of the posterior mediastinal pleura displacement. There is a persistence of the scoliosis at T7 and T8.

The early manifestations of pyogenic osteomyelitis of the thoracic spine seen on a chest roentgenogram are produced by the accumulation of inflammatory material present in the posterior mediastinum, a mediastinitis. It was noted at operation in the case demonstrated that the bed of the eighth rib on the left was indurated a distance of 5 cm. from the spine laterally (Table II).

Table I

Date	Roentgenographic Interpretations	Mediastinal Pleura Displacement in Centimeters				
		Vertebral level				
		T4	T5	T6	T7	T8
8/8/60	Old fracture of the right clavicle. Mediastinum in midline. Heart and lungs normal	Mediastinal pleura not seen				
8/11/60	Lateral displacement of the mediastinal pleura on the left. This is clearly seen through the aortic shadow. The lungs are clear. The mediastinum is in the midline and no soft tissue mass is seen on the right	1.70	2.40	2.40	2.50	2.60
11/5/60	The displaced left mediastinal pleura is more obvious on this examination. There is also a soft tissue mass present in the region of the right hilus. There is a slight scoliosis present. Mediastinum in midline. Lungs clear	2.50	3.00	3.00	3.50	
11/14/60	The left mediastinal pleura is displaced as before with a right soft tissue mass extending from T6–T9. The left pleura displacement extends from T4–T9					
11/15/60	Barium swallow studies show definite external pressure defect at level T7 and T8 and bone destruction of T7					
12/17/60	Findings similar to 11/14/60. The roentgenograms are slightly overexposed compared with 11/14/60 and the detail of the mediastinum and spine is better. Scoliosis present in mid-thoracic spine	2.50	2.80	3.50	3.70	
12/28/60	Postoperatively, the chest shows partial resection of 8th left rib. Right mediastinal pleura visible extending from T6–T10. This was not observed on previous roentgenograms. Left mediastinal pleura again visible		2.40	2.40	2.50	
2/27/61	Gradual diminution of pleural displacement laterally, the right persisting longer than the left					
6/19/61	Normal chest					

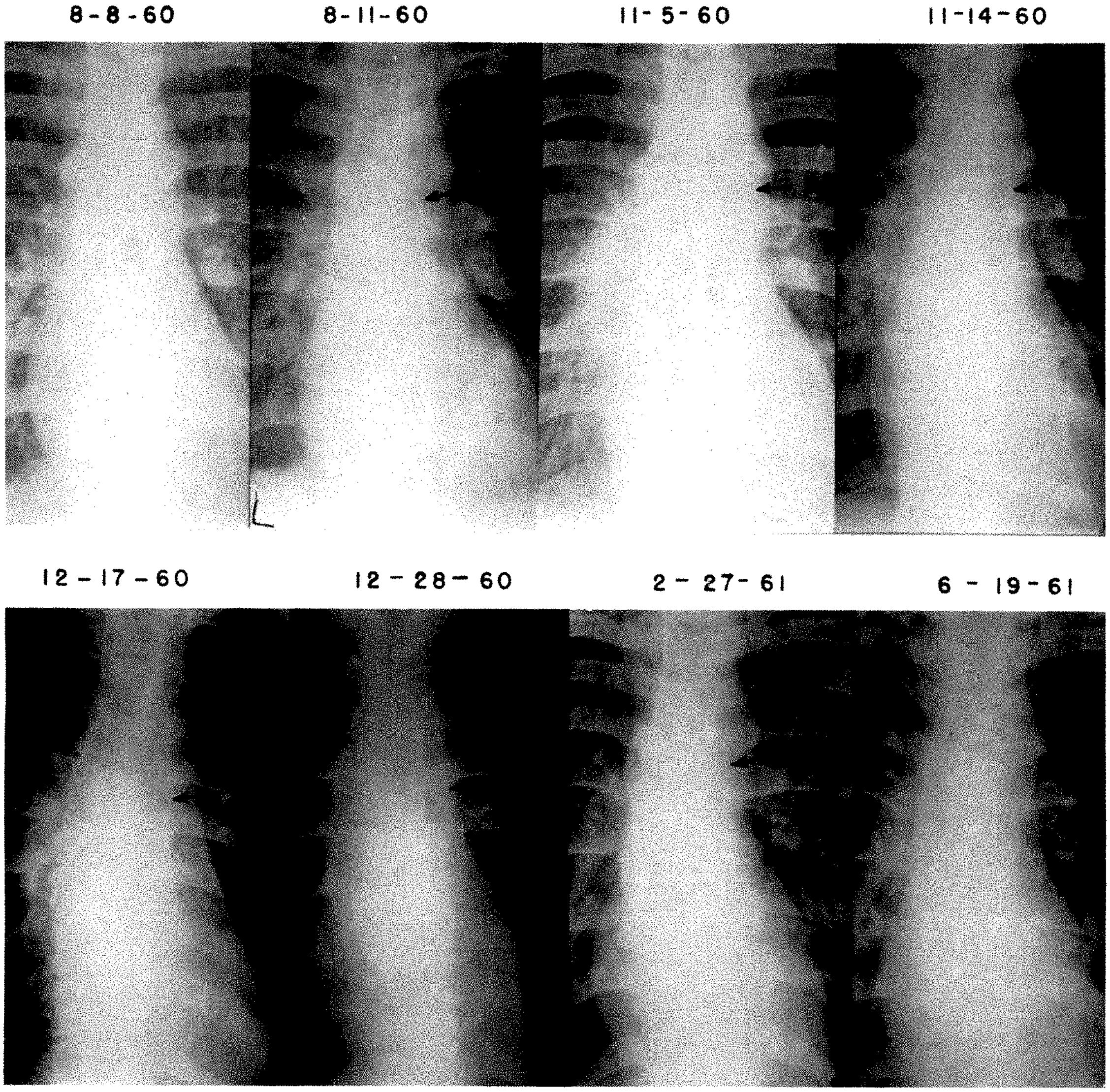


FIG. 1. Linear displacement of the left mediastinal pleura and the gradual appearance of a right paravertebral globular mass.

DISCUSSION

Pyogenic infection of the spine is an uncommon, painful and debilitating disease. In 292 cases of osteomyelitis treated in a single hospital over a 10 year period, the vertebrae were involved in only 10 instances.[7] It appears to be more common in the male than in the female.

The common causative organism is *Staphylococcus aureus*, but *Staphylococcus albus*, *Streptococcus*, *Bacillus typhosus* and *coli*, *Pseudomonas* and the *Brucella* group have been incriminated.[8,9] Osteomyelitis of the spine following urinary tract infections and prostatic surgery is well documented.[2,4,5]

The diagnosis is extremely difficult because of the complexities of the clinical manifestations, and consequently the course of the disease is prolonged.[7,10] The clinical course is characterized by the absence of unimpressive local signs, pain of increasing severity referred to the abdomen, hips or limbs with the temperature frequently normal. Table II lists the protean clinical and laboratory manifestations of the disease. The vagueness and distribution of the pain tends to lead the unsuspecting physician up the proverbial garden path away from the diagnosis.

Needle biopsy has been suggested and utilized, but this is risky and uncertain in the thoracic region.[6] The classic open operation, costotransversectomy, will also establish the diagnosis and provide a specimen to ascertain the antibiotic sensitivity of the infecting organism. The prognosis is good.

The roentgenographic manifestations of pyogenic infections of the spine, and the differentiation between this disease process and a tuberculous infection are well documented.[8,9,10] Wear *et al.*[10] advocated careful history taking, scrutiny of spine roentgenograms, oblique and spot roentgenograms, and laminagrams in the evaluation of early lesions where changes are minimal. However, the lateral displacement of the linear thoracic paraspinal shadow, or the posterior mediastinal pleura, due to a mediastinitis, is a roentgenographic sign which is seen on a properly exposed chest roentgenogram early and before the signs of a paravertebral abscess, bone destruction and proliferation appear in the thoracic region. Although an uncommon condition today, early recognition is of prime importance to avoid prolonged morbidity or even more serious consequences.

TABLE II

Date	Symptoms and Signs	Laboratory Investigation and Treatment
8/8/60	Three days before, fell and hurt right side and complained of pain in epigastrium and lower thoracic spine. Temperature 103.8°F., pulse 104. Very tender right abdomen and lower right ribs	Sedimentation rate 101 mm./hr.
8/11/60	Chest clear. Anorexia but no vomiting. Provisional diagnosis: ruptured appendicitis; viral pneumonia. Pain subsided. Discharged after 12 days	Treatment: chloromycetin with resultant fall in temperature.
11/2/60	Patient complained of right lower thoracic and flank pain becoming progressively severe over a few days. No chills. Temperature 98.6°F. Lungs clear. Right flank tender. Few white blood cells in urine	Treatment: gantresin
11/3/60	Patient complained of severe pain in right anterior rib margin. Temperature 100°F., pulse 102. Slight epigastric tenderness. Lungs clear. Patient was restless and grimacing from pain. A stiff neck was also present. Admitted to hospital. Diagnosis: (1) right pneumonia and right subphrenic abscess; (2) Salmonella enteritis; (3) osteitis pubis; (4) pleurodynia myositis; (5) lymphoma; (6) hepatic contusion	Moderate eosinophilia. Lumbar puncture normal. Serology normal. Liver function tests normal. Agglutination tests normal. No treatment. Discharged. The patient improved after 11 days
11/21/60	Seen in physician's office. Well, no complaints. Lungs clear and allowed to return to work	
12/13/60	Seen in physician's office. Complaining of left posterior paravertebral pain with tenderness at level of T6. Lungs clear	Treatment: local injection of xylocaine producing relief of symptoms
12/16/60	Admitted to hospital. Severe pain in anterolateral chest for 4 days. Pain increased with respiration and twisting and there was stiffness of the midback with nuchal rigidity. Patient was pale, thin and chronically ill with marked spasm in the lumbar region. Motion in the thoracolumbar region was markedly limited in all directions. There was localized tenderness and edema to the left of T12. Examination of chest, abdomen and central nervous system was negative. Temperature normal.	Hemoglobin 13.5 gm. per cent; hematocrit 41.5 per cent; white blood cell count 10,500; polymorphonuclears 57 per cent; lymphocytes 30 per cent; monocytes 5 per cent; eosinophils 2 per cent; sedimentation rate 11 mm./hr.; urinalysis negative; spinal fluid normal; tuberculin test negative through 1/1,000; febrile agglutinins for typhoid, paratyphoid, Brucella and Salmonella negative Treatment: costotransversectomy of left 8th rib. No visible pus. Bed of 8th rib indurated for distance of 2 inches from spine Surgical pathology: (1) culture of bone and cartilage: *Staphylococcus pyogenes* (coagulase positive); (2) fibrosis and subacute and chronic inflammatory exudate

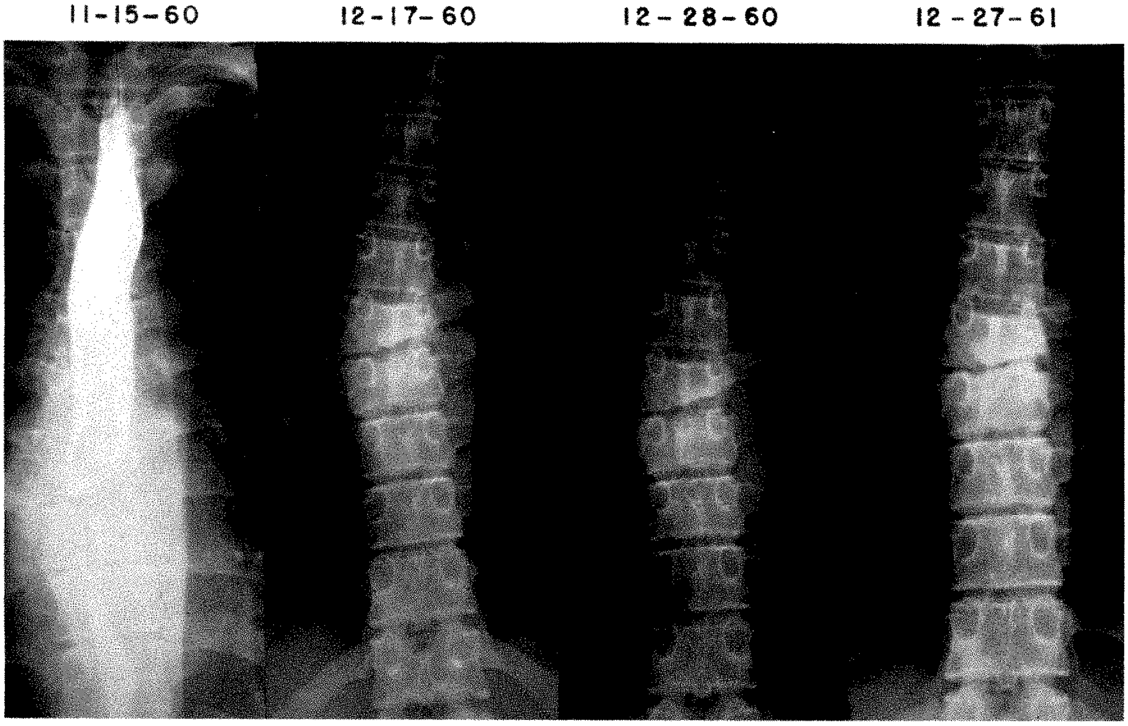


Fig. 2. Bone changes produced by pyogenic infection of the thoracic spine.

SUMMARY

A case of pyogenic osteomyelitis of the thoracic spine, an uncommon but crippling condition, is reported. The complexities of the clinical manifestations which tend to delay the diagnosis are presented. Displacement of the linear thoracic paraspinal shadow or the posterior mediastinal pleura from the midline, an early roentgenographic manifestation of this disease, and the later development of the classic late signs of osseous involvement are demonstrated.

Department of Radiology
Massachusetts General Hospital
Boston 14, Massachusetts

REFERENCES

1. Brailsford, J. F. Radiographic postero-medial border of lung, or linear thoracic paraspinal shadow. *Radiology*, 1943, *41*, 34–37.
2. De Feo, E. Osteomyelitis of spine following prostatic surgery. *Radiology*, 1954, *62*, 396–401.
3. Editorial. Linear thoracic paraspinal shadow. *Radiology*, 1942, *39*, 229.
4. Leigh, T. F., Kelly, R. P., and Weens, H. S. Spinal osteomyelitis associated with urinary tract infections. *Radiology*, 1955, *65*, 334–342.
5. Liming, R. W., and Youngs, F. J. Metastatic vertebral osteomyelitis following prostatic surgery. *Radiology*, 1956, *67*, 92–94.
6. Rix, R. Personal communication.
7. Robinson, B. H. B., and Lessof, M. H. Osteomyelitis of spine. *Guy's Hosp. Rep.*, 1961, *110*, 303–318.
8. Schinz, H. R., Baensch, W. E., Friedl, E., and Uehlinger, E. Roentgen-Diagnostics. Vol. II. Skeleton. Grune & Stratton, New York, 1952.
9. Ting, Y. M. Osteomyelitis of spine. *Radiology*, 1961, *76*, 27–31.
10. Wear, J. E., Baylin, G. J., and Martin, T. L. Pyogenic osteomyelitis of spine. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1952, *67*, 90–94.

VERTEBRAL EPIPHYSITIS: A COMPARISON OF THE CLINICAL AND ROENTGENOLOGIC FINDINGS*

By HUGH J. WILLIAMS, M.D., *Fellow in Radiology and* DAVID G. PUGH, M.D.,
Section of Roentgenology
MAYO CLINIC AND MAYO FOUNDATION
ROCHESTER, MINNESOTA

INASMUCH as vertebral epiphysitis is more prevalent than generally appreciated, it seemed worthwhile to review and to compare the roentgenologic and the clinical findings during the active phase of this disease. Additional purposes of this investigation were to determine how many adolescents with roentgenologic signs of active vertebral epiphysitis (Scheuermann's disease) present clinical evidence of this disease and finally to determine how many adults with roentgenographic evidence of earlier epiphysitis had had clinical signs or symptoms of the disease in its active phase.

HISTORICAL BACKGROUND

In 1921, Scheuermann[7] first described the clinical and roentgenologic findings in 105 cases of juvenile kyphosis (vertebral epiphysitis). He was the first to differentiate this type of kyphosis from the rachitic and postural kyphosis of children. He emphasized the need for roentgenologic examination of the spinal column in diagnosing juvenile kyphosis and noted that irregularity of the vertebral epiphyses, which is the most prominent roentgenographic feature in this condition, was absent in all other types of kyphosis. He expressed the view that disturbances of the vertebral growth centers were due to isolated severe trauma or repeated minor trauma.

Schmorl,[8] in 1930, published his conclusions regarding the pathogenesis of juvenile kyphosis after postmortem study of hundreds of spinal columns. He described minute fissures in the cartilaginous plates of the involved vertebrae through which herniations of the substance of the nucleus pulposus into the spongiosa of the vertebrae occurred. He stated that, as a result of a loss of the disk substance, the cushioning function of the disk was so disrupted that an excessive strain was imposed on the anterior aspect of the involved vertebral bodies which resulted in wedging.

In 1931, Beadle,[1] after a comprehensive and detailed postmortem study, described three stages in the development of vertebral epiphysitis. First, some inborn weakness or developmental error had resulted in defects in the cartilaginous plates of the involved vertebrae. These defects, which consisted of minute fissures, occurred most frequently in the thoracic or lumbar vertebrae, often in several adjacent vertebrae. These defects in themselves did not produce the disease, but they served as potentially weak foci through which the nucleus pulposus could prolapse into the spongiosa of the neighboring vertebrae following undue stress such as that of prolonged manual labor, strenuous sports, or habitual bending postures. Herniation of the nucleus pulposus, the second phase of the development of the disease, did not necessarily cause deformity unless continuous strain was imposed on the cartilaginous plates by excessively hard work or sports activities. With continuation of these excessive stresses, the third and deforming phase of the disease occurred; namely, the growth disturbance phase. Due to passage of a portion of the nucleus pulposus into the vertebral body or bodies (the second phase), the efficiency of the intervertebral disk as a pressure-equalizing structure was considerably diminished. Because of the normal thoracic curvature, the anterior portion of the underlying vertebra was subjected to more pressure than the posterior portion, resulting in decreased endochondral bone formation anteriorly. This disparity in the rates of growth of endochondral bone between the anterior and posterior portions of the involved vertebrae led to anterior wedging with subsequent development of the typical kyphotic deformity. In addition, the reduced volume of the disk, resulting from passage of a portion of the nucleus pulposus into the spongiosa, caused narrowing of the intervertebral space. Beadle[1] emphasized that all three causal elements had to be present to produce kyphosis. The developmental disposition did not lead to production of the disease unless the excessive physical stresses were imposed, and even prolapse of the disk did not necessarily result in kyphosis unless the undue stresses were sufficiently prolonged to interfere with growth of endochondral bone.

---

* Abridgment of thesis submitted by Dr. Williams to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Radiology.

Ehrenhaft,[4] in 1943, by careful study of the vertebral column during and after embryologic development, determined that the epiphyseal ring did not play a role in the vertical growth of the vertebral body. This growth in height is exclusively a function of the cartilaginous plates which are central to the epiphyseal rings and constitute the superior and inferior aspects of the vertebral bodies.

In 1950, Bick and Copel,[2] after performing longitudinal dissections on numerous spinal columns, reached a similar conclusion and stated that longitudinal growth of the vertebral column resulted solely from endochondral development through the cartilaginous plates. They emphasized that since the epiphyseal ring did not contribute to longitudinal growth of the vertebra, it should more correctly be called the "vertebral ring."

Wassman,[9] in 1951, found evidence of Scheuermann's disease in 5 per cent of 581,000 Danish recruits of conscription age (about 20 years) examined during the years 1922 to 1939. He found that the incidence of the disease was eight times more prevalent in rural than in urban recruits. Moreover, most of the urban recruits with the disease had engaged in heavy manual work. He concluded that the principal cause of vertebral epiphysitis was the stress of physical labor during adolescence.

Dameron and Gulledge,[3] in 1953, examined 1,000 naval recruits between the ages of 17 and 23 years and found that 61 (6 per cent) demonstrated clinical or roentgenologic evidence of Scheuermann's disease. Only 7 per cent gave a history of any trauma to the back, and only 12 per cent recalled having had any previous backache.

In 1955, Ferguson[6] reiterated a possible etiologic mechanism in Scheuermann's disease, which he first advanced in 1949.[5] He postulated that, when the anterior vascular grooves in the thoracic vertebrae (which normally disappear by the time the child is 6 years old) persist, they result in potentially weakened areas in the involved vertebrae. Such vertebrae then are capable of undergoing anterior wedging, resulting in kyphosis. He stated that kyphosis secondary to this mechanism occurred chiefly in children between the ages of 6 and 10 years, and at a time considerably before the appearance of the epiphyseal rings. The resultant kyphosis disrupted the normal mechanics of the spinal column to such an extent that the ring epiphyses underwent irregular ossification when they finally appeared. He concluded that the presence of vascular grooves which persist in the thoracic vertebrae of adolescents with clinical and roentgenologic evidence of Scheuermann's disease should suggest that the irregularities of the ring epiphyses were secondary to a process which initiated considerably prior to adolescence.

MATERIAL AND METHODS

The patients were divided into two groups. The first group consisted of 100 patients between the ages of 10 and 20 years with roentgenologic evidence of Scheuermann's disease. These age limits

Table I

SEX DISTRIBUTION OF PATIENTS WITH VERTEBRAL EPIPHYSITIS

	Patients with	
	Active Disease	Inactive Disease
Male	68	27
Female	32	23
Total	100	50

were chosen inasmuch as the active form of the disease is uncommon before the child is 10 years of age and is seldom seen after 20 years of age; thus, this group is the group with active disease. Any patient with an associated disease, which could be productive of symptoms similar to those of vertebral epiphysitis, was excluded from this series.

The second group was composed of 50 patients between the ages of 20 and 30 years who had roentgenographic evidence of earlier Scheuermann's disease. The upper age limit was selected as indicated, because hypertrophic changes, which might obscure the clinical and roentgenologic findings, are seldom seen before the person is 30 years old. This group will be referred to as having inactive disease.

RESULTS IN GROUP WITH ACTIVE DISEASE

Sex. Sixty-eight per cent of the patients were males and 32 per cent were females (Table I).

Age at Onset of Symptoms. According to age of patients when they presented themselves, the incidence of symptoms was highest in those 15 and 16 years old (Table II). There were twice as many patients (20) with symptoms in the 17 to 20 year old group as in the 10 to 14 year old group (10).

Symptoms. The presenting symptom of 48 patients was pain. In an additional 4 patients, increasing thoracic kyphosis unassociated with pain was the causative factor in their seeking medical attention. Thus, 52 per cent of patients with the active disease had clinical manifestations of the disease, while 48 per cent were asymptomatic with the changes being found incidentally because of roentgen examinations for other reasons. In 40 of the 48 patients who complained of pain, the pain was localized over the involved vertebrae. In 6 patients, the thoracic region was the site of the disease, but the pain was distributed in the lumbar region. In 1 patient with lumbar involvement, the pain was noted in the right sacroiliac joint. Lumbosacral pain occurred in 1 patient in whom the disease was located in the lower thoracic and upper lumbar vertebrae. Extension of the pain into the thighs occurred in 2 patients with lumbar involvement, but no extension was noted in any patients with thoracic involvement. In 12 patients the pain was aggravated by exercise and relieved by rest. Some limitation of movement of the spinal column was evidenced by 7 patients. Tenderness on pressure over the involved vertebrae, when recorded by the examining physician, was described as dull in 9 cases and sharp in 1. The nature of the pain was mild in 9 cases, moderate in 7, and severe in 2. In the remainder the character of the pain was not specified. No correlation was apparent between the severity of the pain

Table II

AGE OF PATIENTS WITH ACTIVE DISEASE SYMPTOMS AT TIME OF ADMISSION

Age (yr.)	No.
10	1
11	2
12	0
13	2
14	5
15	9
16	13
17	6
18	7
19	5
20	2
Total	52

and the roentgenologic findings, but pain was commoner in patients with kyphosis than in those with no deformity.

Antecedent Trauma. In 16 cases a history of trauma to the back preceding the onset of symptoms was elicited. In 1 patient who struck his back during a fall, roentgenograms made immediately afterward showed no abnormality. Six weeks after the fall, pain developed in the thoracic region of the back and became progressively more severe until he visited his physician 9 months later. Roentgenologic examination of the spinal column at this time revealed well-developed epiphysitis in the thoracic region.

Vertebral Involvement (*Table* III). Involvement of multiple vertebrae occurs most frequently; in 49 per cent of the cases, 5 or more vertebrae presented roentgenographic evidence of Scheuermann's disease.

The incidence of the disease in the last 5 thoracic vertebrae was almost the same (Table IV). The incidence of involvement dropped progressively in the vertebrae that were more cephalad and the first 3 thoracic vertebrae were not involved. In the lumbar region the first lumbar vertebra was involved most commonly, and a progressive decrease in frequency of involvement was found in subsequent lumbar vertebrae (Table IV).

Table III

NUMBER OF VERTEBRAE INVOLVED AND REGION OF INVOLVEMENT

	Patients with	
	Active Disease	Inactive Disease
Vertebrae Involved		
1	9	1
2	12	4
3	14	12
4	16	12
5 or more	49	21
Region of Involvement		
Thoracic	46	23
Lumbar	16	5
Both	38	22

Table IV

FREQUENCY OF INVOLVEMENT OF THORACIC AND LUMBAR VERTEBRAE

Vertebrae Involved	Patients with		Total
	Active Disease	Inactive Disease	
T-4	2	2	4
T-5	10	5	15
T-6	31	3	34
T-7	39	16	55
T-8	50	27	77
T-9	53	23	76
T-10	51	18	69
T-11	52	19	71
T-12	52	20	72
L-1	41	20	61
L-2	33	14	47
L-3	24	9	33
L-4	20	7	27
L-5	5	3	8

Laboratory Findings. The sedimentation rate, leukocyte count, and differential count were performed in the majority of cases and were normal for all patients except 1 with a concurrent respiratory infection.

Roentgenologic Findings. The roentgenologic features showed considerable variation, but certain findings such as the irregularity of the superior and inferior surfaces of the involved vertebral bodies were noted consistently. For purposes of organization these findings were subdivided accordingly: (1) vertebral rings (epiphyses), (2) the vertebral bodies, (3) the intervertebral spaces, and (4) spinal deformity.

(1) Vertebral Rings (Epiphyseal Rings, Ring Epiphyses). Schmorl and others conclusively demonstrated that vertebral body growth is a function entirely of the cartilaginous plates constituting the superior and inferior aspects of the vertebral body and that the peripherally situated epiphyseal rings play no role in growth. Scheuermann noted that in lateral roentgenograms of the

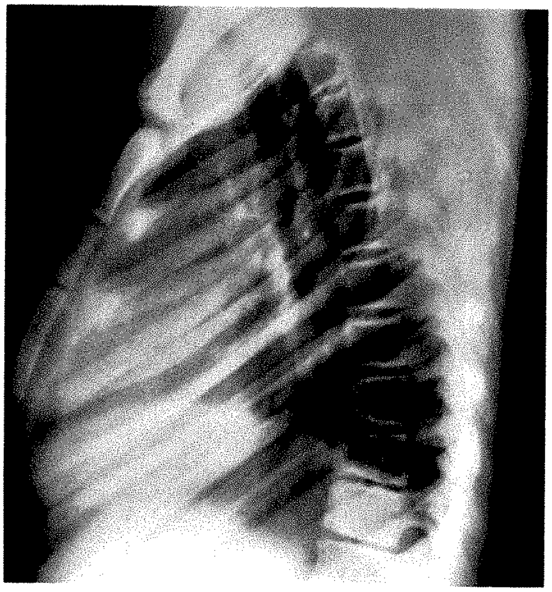


FIG. 1. The normal upper thoracic vertebrae contrast sharply with the involved lower thoracic vertebrae in this case of active epiphysitis. In the latter, Schmorl's nodes, narrowed intervertebral spaces, and fragmentation of the vertebral rings are present.

spinal column the epiphyseal rings appeared as a fine linear density closely paralleling the superior and inferior surfaces of the vertebral body and terminating anteriorly and posteriorly in a small triangular structure due to tangential visualization at these sites. He called the small triangular extremities of the epiphyseal rings the "limbus nucleus" and the remainder of the ring the "limbus." This terminology has not found common acceptance, and hence will not be used in this study. In 74 per cent of our patients the vertebral rings, instead of being continuous and homogeneous, were fragmented (Fig. 1). In addition to fragmentation, 68 per cent of the vertebral rings also showed thickening of varying degrees (Fig. 2 and 3). Enlargement and irregularity of the upper and lower recesses located on the anterior aspects of the vertebral bodies, and in which the anterior portion of the ring epiphyses develops, were noted in 21 per cent of the patients. This enlargement produced a deficiency in the anterosuperior or antero-inferior aspects of the involved vertebrae (Fig. 4). Either an enlarged, bulbous ring epiphysis occupied this deficiency or the ring epiphysis was not apparent due to a delay in developing. Delayed fusion of the ring epiphysis was not uncommon. Less frequently a delayed development of all or a portion of the ring epiphysis occurred.

(2) Vertebral Bodies. The superior and inferior surfaces of the involved vertebrae were frequently hazy and indistinct, reflecting defective development of the cartilaginous epiphyseal plates and resultant malformation of the underlying vertebral bony surfaces (Fig. 5). Schmorl's nodes (Table v) were apparent in routine roentgenograms (anteroposterior and lateral views) in 61 per cent of the cases. In general, they were best detected in the lateral view, but in a considerable number of cases they were also apparent in the anteroposterior view. In a small percentage of cases the nodes were demonstrated best in the anteroposterior view. Schmorl's nodes were present in the thoracic vertebrae of 33 per cent of the

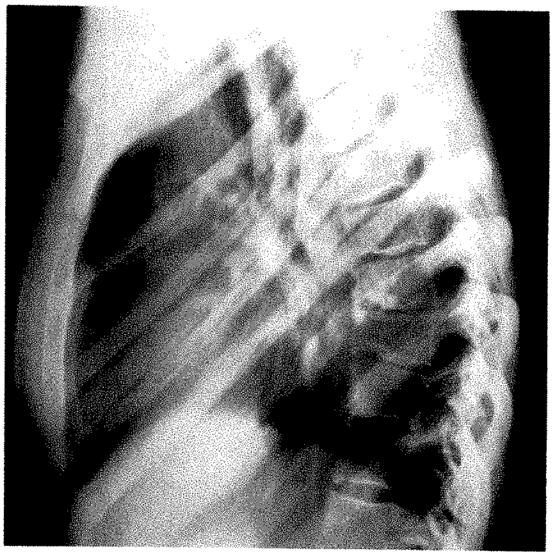


FIG. 2. Active epiphysitis with thickening and fragmentation of several lower thoracic vertebral rings. T-8 and T-9 show moderate anterior wedging. Narrowed interspaces and Schmorl's nodes are also evident. This patient complained of pain in the lower thoracic and upper lumbar regions (no lumbar involvement).

patients, and tended to involve multiple vertebrae rather than a single vertebra. The nodes occurred in the lumbar vertebrae in 13 per cent of the patients, but in this location they tended to be single rather than multiple (Fig. 6). In 15 per cent of the patients the nodes were present in both the thoracic and lumbar vertebrae. Prolapse of the nucleus pulposus through the cartilaginous vertebral plate occurred most commonly in the central region of the vertebral body but was not uncommon in the anterior or the posterior portion. In some cases several prolapses were apparent in different locations in the same vertebral body.

Wedging of the vertebral bodies (Table v) was most frequent in the thoracic region. This probably occurred because the natural kyphos present there imposed increased pressures on the anterior aspects of the vertebral bodies due to herniation of the nucleus pulposus and resultant loss of the cushioning properties of the disk. This abnormal pressure on the anterior portion of the vertebra produced diminished growth in the anterior portion as compared to the posterior portion and resultant anterior wedging of the vertebral body. In the thoracic vertebrae wedging occurred in 41 per cent of the patients, and multiple vertebrae were more commonly involved than a single vertebra. Wedging occurred in the lumbar region in 11 per cent of the patients where single involvement was commoner than multiple involvement. Wedging occurred in both the thoracic and lumbar regions in 7 per cent of the patients.

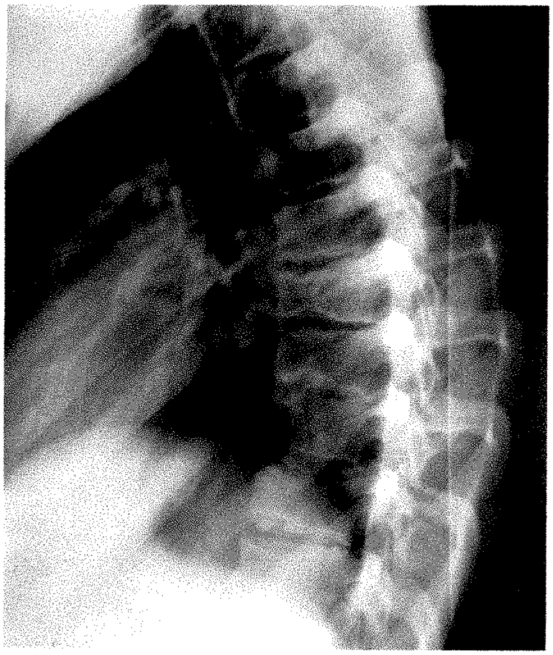


Fig. 3. Thickening, fragmentation, and delayed development of the vertebral rings are all evident in the lower thoracic vertebrae. The superior and inferior surfaces of the vertebral bodies are irregular and indistinct. Several vertebrae contain Schmorl's nodes. T-7 is wedged. The patient was in the active phase of the disease and was asymptomatic. Contrast this with Figure 2 as that patient had pain and a similar degree of involvement.

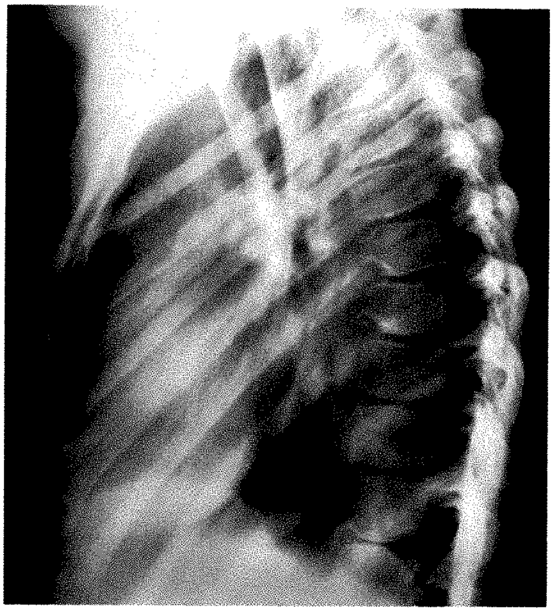


Fig. 4. Active epiphysitis. Deficiency in the antero-superior and antero-inferior aspects of the bodies of several vertebrae.

Vascular channels which persisted were found in one or more of the involved vertebral bodies in 24 per cent of the patients. In a small percentage of patients, a persistent vascular channel was demonstrable in a collapsed vertebra.

(3) Intervertebral Spaces. Narrowing of one or more of the intervertebral spaces was evident in 28 per cent of the patients. This narrowing occurred more commonly be-

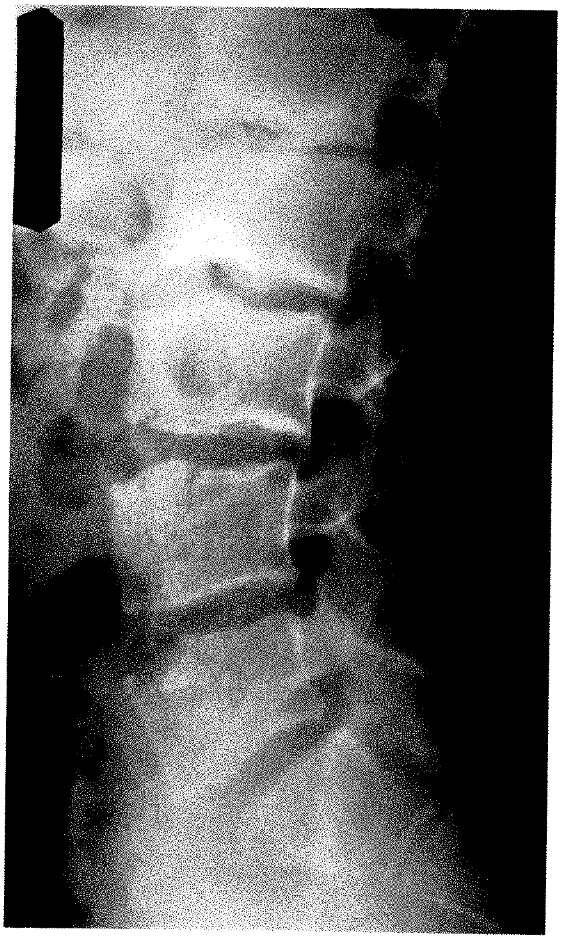


Fig. 5. Active lumbar epiphysitis with indistinct, superior and inferior surfaces of the vertebral bodies. Thickening and fragmentation of the vertebral rings are also present. Several vertebrae contain Schmorl's nodes.

tween the thoracic than between the lumbar vertebrae. Indistinctness and haziness of adjacent vertebral surfaces were common findings particularly in the presence of considerable thickening and fragmentation of the vertebral rings.

(4) Spinal Deformity. Kyphosis occurred in 24 per cent of the patients (Table vi). As expected, it was much more common in the thoracic region (22 patients) than in the lumbar (2 patients). The kyphotic deformity in the thoracic region spanned from 2 to 4 vertebrae, and in all but 1 case the deformity occurred between the sixth and tenth thoracic vertebrae. Scoliosis was found in 23 per cent of the patients (Fig. 7) and occurred predominantly in the thoracic region. Pain was present in 66 per cent of patients with kyphosis in contrast to 42 per cent of patients without kyphosis.

Miscellaneous Findings. Three of the patients presented findings which are worthy

Table V

DISTRIBUTION OF PATIENTS AND LOCATION OF SCHMORL'S NODES AND VERTEBRAL WEDGING

Location and No. of Vertebrae Involved	Patients with			
	Schmorl's Nodes		Wedging	
	Active Disease	Inactive Disease	Active Disease	Inactive Disease
Thoracic	33	17	41	19
single	9	8	16	11
multiple	24	9	25	8
Lumbar	13	9	11	3
single	10	6	7	3
multiple	3	3	4	0
Both	15	11	7	4
Total	61	37	59	26

of mention. In the first patient, aged 17 years, considerable hypertrophic changes were superimposed on healing epiphysitis in a thoracic segment of the spinal column (Fig. 8). The second patient had a dense osteoblastic reaction in the vicinity of a Schmorl node which closely simulated the appearance of an infectious spondylitis. The third revealed definite narrowing of one of the thoracic intervertebral spaces, and the anterior aspects of the adjacent involved vertebrae were in close contact with each other. The appearance suggested that anterior fusion of these vertebrae could result.

RESULTS IN PATIENTS WITH INACTIVE DISEASE

Sex. Fifty-four per cent of the patients in this group with roentgenographic evidence of previous Scheuermann's disease were males and 46 per cent were females.

Childhood Symptoms of Vertebral Epiphysitis. Twelve per cent of the patients recalled having had persistent backache in childhood, and half of these had received treatment for vertebral epiphysitis at the time. Only 4 per cent of the patients had backache at the time of examination which was attributed to the previous vertebral epiphysitis. There was no associated kyphosis in any of these symptomatic patients.

Table VI

DISTRIBUTION OF PATIENTS WITH SPINAL DEFORMITY

Type of Deformity and Location	Patients with Active Disease	Patients with Inactive Disease
Kyphosis	24	13
thoracic	22	12
lumbar	2	1
Scoliosis	23	11
thoracic	19	10
lumbar	4	1
Total	47	24

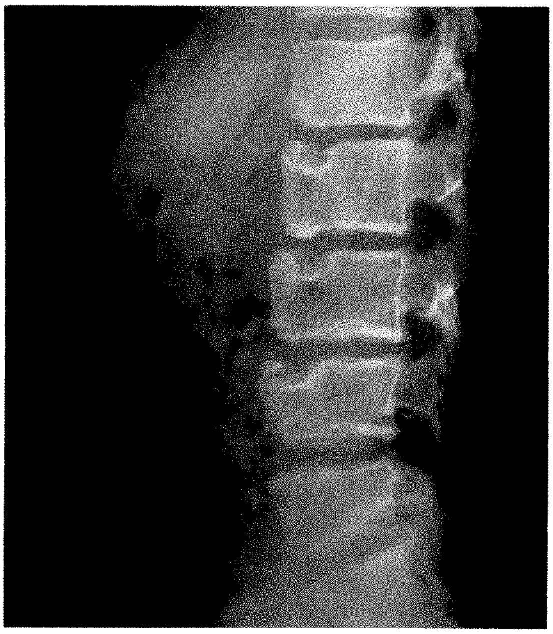


Fig. 6. Active lumbar vertebral epiphysitis with multiple Schmorl's nodes. The nodes are more common in the thoracic vertebrae than in the lumbar. Enlarged bulbous ring epiphyses are present in L-2, L-3, and L-4.

Antecedent Trauma. Of the 6 patients who recalled the presence of the disease in childhood, 4 stated that trauma had occurred prior to onset.

Laboratory Findings. In no case in this group was there any abnormal alteration of

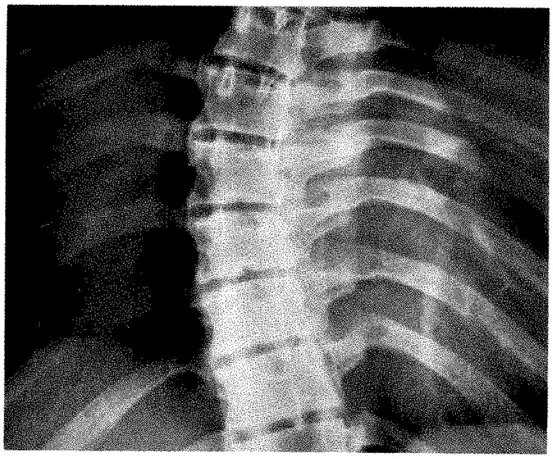


Fig. 7. Active epiphysitis. Right convex scoliosis is prominent. Several vertebrae contain Schmorl's nodes which usually are best seen in a lateral view.

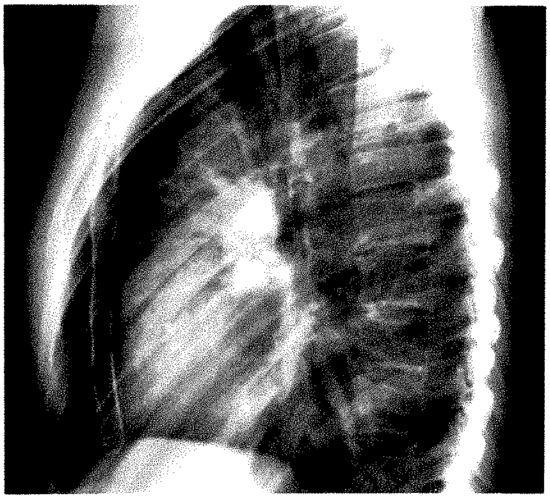


FIG. 8. Hypertrophic changes superimposed on healed vertebral epiphysitis in a 17 year old youth. The irregular, superior, and inferior margins of the vertebral bodies are characteristic sequelae.

the leukocyte count, differential count, or sedimentation rate.

Roentgenologic Findings. (1) Vertebral Rings (Epiphyses). Normally, the vertebral rings (epiphyses) fuse with the vertebral bodies shortly after the cessation of vertebral growth. In 10 per cent of our cases, the failure of at least one ring epiphysis to fuse with the vertebral body produced the characteristic roentgenologic feature of a triangular, ossified structure lying adjacent to the anterosuperior or antero-inferior aspect of the involved vertebra.

(2) Vertebral Bodies. In all patients there was an irregularity of the superior or inferior margins of the involved vertebral bodies (Fig. 9). The degree of irregularity varied among patients and among vertebrae of the same patient. In most patients both the superior and inferior margins of the involved vertebrae were irregular, but involvement of only one of the margins was not uncommon. This marginal irregularity is a manifestation of abnormal endochondral bone formation by the cartilaginous plates of the vertebral body.

Schmorl's nodes (Table V) were present in 74 per cent of the patients. The nodes occurred in the thoracic vertebrae of 34 per cent of the patients and involved a single vertebra or multiple vertebrae with equal frequency. They were found in the lumbar region in 18 per cent of the patients where single vertebral involvement was commoner than multiple involvement. Involvement of both the thoracic and lumbar vertebrae occurred in 22 per cent of patients.

Wedging (Table V) was found in 52 per cent of the patients and occurred most commonly in the thoracic region (38 per cent). Wedging involving single vertebra was slightly more common than that involving multiple vertebrae. In the lumbar region the wedging occurred in 6 per cent of the patients and involved one vertebra in each patient. Combined thoracic and lumbar wedging occurred in 8 per cent of patients. The incidence of lumbar wedging in this group was rather similar to that found in the active group.

Superimposed hypertrophic changes were noted in the involved vertebrae in 42 per cent of the patients and varied from slight to moderately severe.

Persistent vascular channels were found in one or more of the involved vertebral bodies in 8 patients. In each of 2 patients

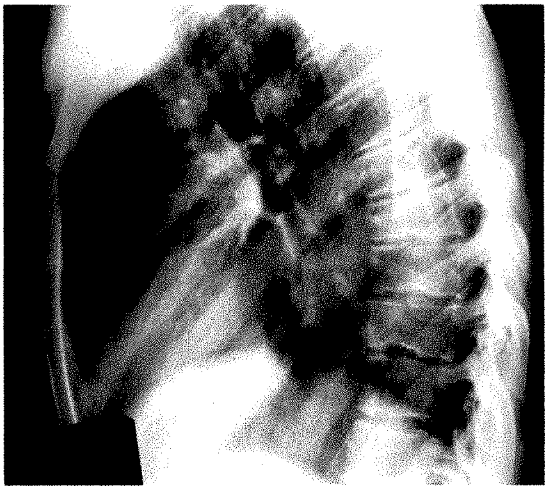


FIG. 9. The lower thoracic vertebrae demonstrate the typical residuum of healed epiphysitis. The irregularities of the superior and inferior margins of the vertebral bodies are typical. T-6 and T-7 show moderate anterior compression and several vertebrae contain Schmorl's nodes.

a persistent vascular channel was identifiable in a collapsed vertebral body.

(3) Intervertebral Spaces. Narrowing of one or more intervertebral spaces in the involved segment was present in 28 per cent of the patients and was commoner in the thoracic region than in the lumbar.

(4) Spinal Deformity. Kyphosis occurred in 26 per cent of patients and was located in the thoracic vertebral region in all but 1 patient; in the exception it occurred in the lumbar region (Table VI). The kyphotic deformity in the thoracic region spanned from 2 to 4 vertebrae, and was located between the sixth and tenth thoracic vertebrae in every case.

Scoliosis was noted in 22 per cent of the patients and was more prevalent in the thoracic region than in the lumbar segment of the vertebral column (Table VI).

COMMENT AND SUMMARY

The clinical and roentgenologic findings in a group of patients with active vertebral epiphysitis and in a group with residual evidence of this disease were compared. The relatively high incidence of this disease in childhood has not been generally appreciated despite studies that have revealed roentgenologic evidence of healed vertebral epiphysitis in 6 per cent of the adults studied.

Etiology. The etiology of this disease is not clearly understood, as evidenced by the number of causative theories advanced. Scheuermann stated that this disease was primary in the vertebral rings, but Schmorl maintained that the irregularity of the vertebral rings was secondary to abnormal mechanical stresses imposed on the spinal column following herniation of the nucleus pulposus into the vertebral bodies. More recent work has suggested that the basic predisposing factor is the presence of minute deficiencies in the cartilaginous plate through which herniation of the nucleus pulposus can occur into the adjacent vertebral body.

Inasmuch as the superior and inferior margins of the vertebral body were frequently indistinct and irregular in the roentgenograms of active cases analyzed in this study, it was thought that a defect in endochondral bone formation by the cartilaginous plate with the resultant prolapse of the nucleus pulposus through this imperfectly formed bone was a probable etiologic factor in this disease.

The role of persistent anterior vascular channels in the production of the disease in this study was difficult to evaluate, although their presence was noted in 24 per cent of the involved vertebrae. It seemed unlikely, however, that they played a prominent role in the mechanism of the disease in most cases.

The role of antecedent trauma also was difficult to evaluate because of its relative frequent occurrence in most children. No attempt was made to relate the disease with the nature of the patient's occupation because past investigations have revealed an increased incidence of this disease in adolescents engaged in manual labor or strenuous play.

Symptoms. In the active group 48 per cent of the patients had pain as the presenting symptom, and an additional 4 per cent had noted increasing, but painless, thoracic kyphosis. The incidence of pain in the active group was considerably higher than that found in most mass "back surveys" of patients in this age group, since the very presence of pain prompted the clinical and roentgenologic examination in many of our patients. In the remainder the disease was discovered incidentally on roentgenograms taken for other reasons. The pain was localized to the involved segment of the spinal column in 40 of the 48 patients and was usually mild. Pain extended to the thighs or to another portion of the vertebral column in only 2 patients. No correlation existed between the severity of the pain and the extent of roentgenologic findings. Pain, however, was more common in patients with thoracic kyphosis than in those with no deformity.

Only 12 per cent of the patients with inactive disease were symptomatic during the active phase of the disease. This figure is in agreement with that of Dameron and Gulledge[3] and probably represents the actual incidence of symptoms during the active phase of vertebral epiphysitis. This relative infrequency of pain during the active phase (88 per cent) is worthy of stress, and explains why the number of active cases presenting clinically is small despite the relatively high incidence of the disease in children (6 per cent).

Laboratory Findings. No alteration of the sedimentation rate, leukocyte count, or differential count occurred in any of the patients with vertebral epiphysitis.

Roentgenologic Findings. Multiple vertebrae were involved in the majority of patients in both groups; in 49 per cent of the patients with the active disease, 5 or more vertebrae were involved. Thoracic involvement occurred most frequently; a combination of thoracic and lumbar involvement was next most frequent and lumbar involvement alone was least common. Cervical vertebrae were not involved by the disease in any of the cases studied.

During the active phase of the disease the characteristic roentgenologic findings were as follows: The epiphyseal rings demonstrated irregularity, enlargement, and fragmentation, and less commonly, delayed development. The superior and inferior surfaces of the involved vertebrae were frequently indistinct and irregular, indicating abnormal endochondral bone formation by the cartilaginous plate. In 21 per cent of the patients, a defect occurred in the vertebral body at the site of the recess where the anterior portions of the epiphyseal ring develop. Wedging of the vertebral bodies was observed in 59 per cent of the patients, with the highest incidence in the thoracic region where it tended to involve multiple vertebrae. Schmorl's nodes occurred in 61 per cent of the patients and were more common in the thoracic than in the lumbar vertebrae. The nodes usually involved multiple vertebrae in the thoracic region but single vertebrae in the lumbar region.

Narrowing of one or more intervertebral spaces in the involved segments of the vertebral column occurred in 28 per cent of cases. In several active cases the roentgenologic findings were similar to those produced by traumatic or infectious disease of the spinal column, but the involvement of multiple vertebra in vertebral epiphysitis was the feature that helped distinguish it from the other conditions.

In the group with the inactive disease, the most characteristic roentgenologic finding was an irregularity of the superior and inferior surfaces of the vertebral bodies. Schmorl's nodes, wedging, and narrowing of the intervertebral spaces were noted in approximately the same percentage of patients as in the group with the active disease. Hypertrophic changes of varying degree were superimposed in the involved segment of the spinal column in 42 per cent of the cases, as opposed to only 1 per cent in the group with the active disease. Inasmuch as degenerative arthritis is relatively uncommon in persons less than 30 years of age, it was evident that these hypertrophic changes were secondary to vertebral epiphysitis. The presence of osteoarthritis in the spinal column of an individual less than 30 years of age in the absence of evidence of trauma, infection, or congenital deformity should, therefore, direct attention to the possibility of a pre-existing epiphysitis and prompt a careful search for the characteristic findings of this disease.

Kyphosis occurred in approximately 26 per cent of the cases in both groups, and was nearly always found in the thoracic region. The kyphotic deformity tended to span from 2 to 4 vertebrae and occurred between the sixth and tenth thoracic vertebrae in all but one patient.

Scoliosis, seldom extensive in nature, occurred in approximately 23 per cent of the cases in both groups and was observed predominantly in the thoracic region.

The Mayo Clinic
Rochester, Minnesota

REFERENCES

1. Beadle, O. A. The intervertebral discs: Observations on their normal and morbid anatomy in relation to certain spinal deformities. *M. Res. Council*, 1931, *161*, 1–79.
2. Bick, E. M., and Copel, J. W. Longitudinal growth of the human vertebra: A contribution to human osteogeny. *J. Bone & Joint Surg.*, 1950, *32-A*, 803–814.
3. Dameron, T. B., Jr., and Gulledge, W. H. Adolescent kyphosis. *U. S. Armed Forces M. J.*, 1953, *4*, 871–875.
4. Ehrenhaft, J. L. Development of the vertebral column as related to certain congenital and pathologic changes. *Surg., Gynec. & Obst.*, 1943, *76*, 282–292.
5. Ferguson, A. B. Roentgen Diagnosis of the Extremities and Spine. Second edition. Paul B. Hoeber, Inc., New York, 1949, pp. 519.
6. Ferguson, A. B., Jr. Symposium on pediatric orthopedics: Dorsal wedging round back in preadolescents. *Pediat. Clin. North America*, 1955, *2*, 951–956.
7. Scheuermann, H. Kyphosis dorsalis juvenilis. *Ztschr. f. orthop. Chir.*, 1921, *41*, 305–317.
8. Schmorl, G. Die Pathogenese der juvenilen Kyphose. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1930, *41*, 359–383.
9. Wassmann, K. Kyphosis juvenilis Scheuermann—an occupational disorder. *Acta orthop. scandinav.*, 1951, *21*, 65–74.

* * *

THE ROENTGENOGRAPHIC ASPECTS OF PSEUDOGOUT (ARTICULAR CHONDROCALCINOSIS)*

AN ANALYSIS OF 20 CASES

By DANIEL J. McCARTY, Jr., M.D.,† *and* MARVIN E. HASKIN, M.D.‡
PHILADELPHIA, PENNSYLVANIA

"PSEUDOGOUT" is a term recently coined to designate a syndrome characterized by the presence of calcium pyrophosphate crystals in the aspirate from affected joints.[3,5] We have studied 20 patients with this condition; the first 7 cases were reported previously and were first discovered by identification of the characteristic crystal in the synovial fluid, the last 13 cases were found mostly by roentgenographic patterns characteristic of the condition. These patterns consist of calcification (1) of fibrocartilaginous structures, which usually are involved bilaterally, (2) of articular (hyaline) cartilage, which often is involved bilaterally, and (3) of articular capsule. Microscopic examination of calcifications obtained at necropsy has shown that they are composed of microcrystals, morphologically identical to those previously described in synovial fluid. X-ray diffraction powder patterns of these crystals (the "fingerprint" of a crystal) are identical with those obtained from crystals harvested from synovial fluid.[4] The spectrum of articular calcifications described here is identical with that of a condition described as a clinical entity in 1960 by Zitnan and Sitaj.[10] They defined the condition largely by its roentgenographic manifestations and called it "chondrocalcinosis polyarticularis (familiaris)." We recently summarized the roentgenologic findings in 51 reported cases in the world literature.[5]

This communication presents a brief résumé of the features of pseudogout, emphasizing the roentgenographic characteristics.

CLINICAL FEATURES

Twelve men and 8 women comprised this series; 14 were Caucasian and 6 were Negro. Of the Caucasian group, 3 were of Italian, 6 of Jewish, 2 of German and 3 of Anglo-Saxon extraction. The ages of the patients ranged from 42 to 83 years; the mean age of the men was 67.3 years, of the women, 64.1 years. The diagnosis was first made by synovial fluid examination in 8 cases, by roentgenographic examination in 12 cases. At least one well documented attack of acute arthritis occurred in 16 cases; 12 cases had signs and symptoms of degenerative arthritis in the knees. These changes were of sufficient severity in 3 cases to suggest the diagnosis of neurotrophic (Charcot's) joint. In none, however, could this diagnosis be supported by neurologic or serologic evidence of lues. Acute attacks involved the knees most commonly, but occurred in many other joints as well. Large joints such as the hip, shoulder, elbow, wrist and ankle were involved much more frequently than small joints. One patient had experienced only one attack in a lifetime while others had had hundreds of attacks. The diagnosis of gout had been entertained strongly in 9 cases; some were

---

* From the Department of Radiology, Philadelphia General Hospital, Philadelphia, Pennsylvania, and Rheumatology Section, Department of Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania.

Supported in part by Training Grant #2A-5201 and Research Grant #A-4626, National Institute of Arthritis and Metabolic Diseases, U.S.P.H.S., Bethesda, Maryland, and research grant from the Philadelphia chapter of the Arthritis and Rheumatism Foundation.

† Head, Section of Rheumatology, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania. Chief, Arthritis Clinic (Division B), Philadelphia General Hospital. John and Mary R. Markle Scholar in Medical Science.

‡ Staff Radiologist, Department of Radiology, Philadelphia General Hospital.

diagnosed as having rheumatoid arthritis, and others as having degenerative joint disease.

The duration of an attack varied from several hours to several weeks. Recurrent attacks showed a predilection for previously involved joints. The onset of the attack was sometimes explosively sudden, but more often 24 to 48 hours elapsed between the first recognition of pain and its zenith.

Synovial fluid aspirated from acutely affected joints was almost invariably of the inflammatory type, *i.e.*, opaque due to a high leukocytic count and of low viscosity. Microscopic inspection of a "wet smear" of synovial fluid by phase contrast and polarized light microscopy[5] revealed rod-shaped and rhombic crystals, many of which were intraleukocytic. These showed a weakly positive birefringence (sodium urate crystals show strongly negative birefringence). Fluid obtained from chronically involved joints was of the noninflammatory type and often contained crystals which were extraleukocytic. In 6 fluids from such cases, crystals were present in sufficient number to make the fluid opalescent upon gross inspection.

Eight patients were hypertensive; 5 had symptoms due to this disease. Many had evidence of atherosclerosis. Three were overtly diabetic and 3 others had diabetic glucose tolerance tests. Others gave a history of diabetes mellitus in their immediate blood relatives.

It is not known whether or not the acute attacks respond to colchicine. Large doses of salicylates, phenylbutazone, corticosteroids and ACTH all appear to be quite effective in treatment.

There are several instances of familial involvement in the literature; Zitnan and Sitaj[10] have used the term "familiaris." In this series, Case 19 is the daughter of Case 10.

LABORATORY FINDINGS

The serum uric acid level was elevated in 5 cases; there was no abnormality of the serum calcium, phosphorus or alkaline phosphatase. Urinary calcium excretion was abnormally high in one case; this individual also had suffered from a urinary calculus. Tests for homogentisic acid were negative.

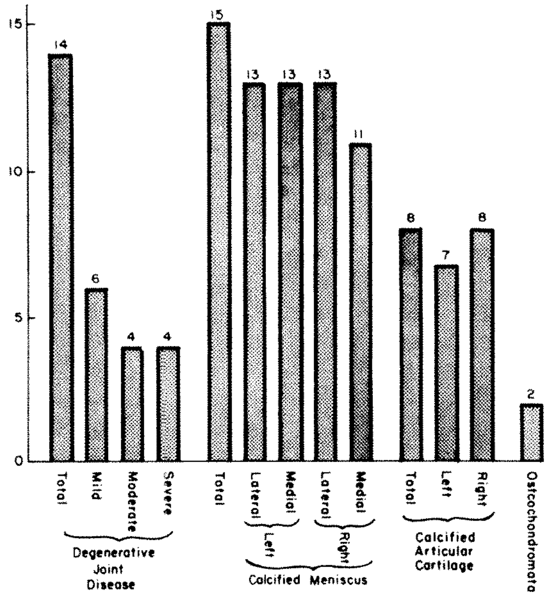


FIG. 1. Roentgenographic findings in the knees of 20 cases of "pseudogout." Bilateral calcification of the menisci was noted in 5 cases without roentgenographic signs of degenerative joint disease.

ROENTGENOGRAPHIC FINDINGS

The knee was involved most frequently; 15 of the 20 cases showed findings typical of the disease in this joint. Figure 1 graphically depicts the frequency of degenerative joint disease (14 cases), calcification of the menisci (15 cases) and calcification of articular cartilage (8 cases). Osteochondroma was seen in the suprapatellar area in 2 instances; 4 additional cases showed intra-articular radiodensities thought to represent "joint mice."

Degenerative changes were felt to be "severe" in 4 cases; 3 of these suggested the diagnosis of neurotrophic (Charcot) joint (Fig. 2, *A* and *B*). Four cases showed moderate and 6 cases showed mild evidence of degenerative joint disease. Meniscal calcification usually involved both the medial and lateral meniscus of both knees in a

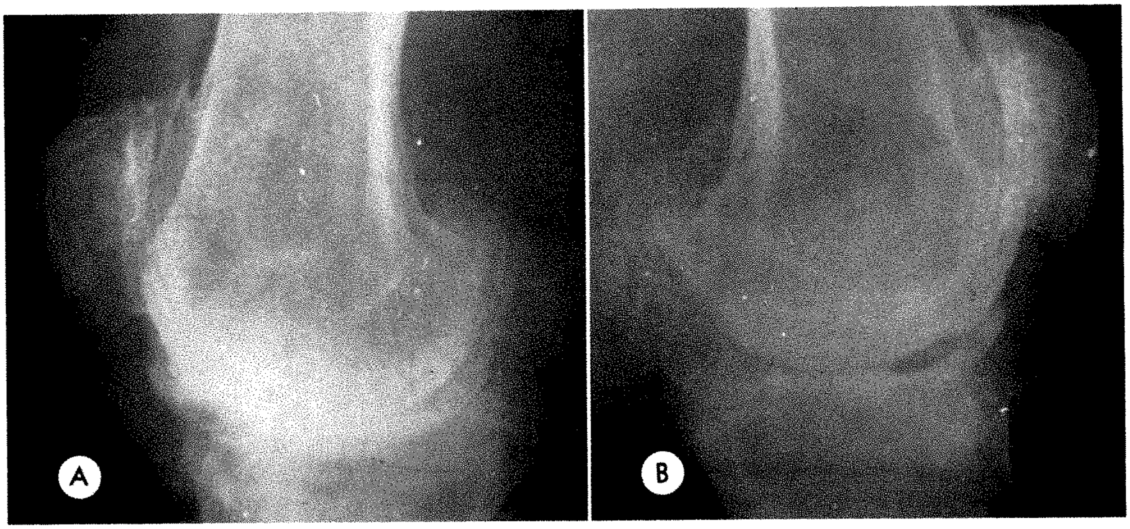


Fig. 2. (*A* and *B*) Pseudogout patient showing severe degenerative changes.

given case; in 3 cases calcification involved the menisci of one knee only. Five cases showed bilateral calcification of menisci without roentgenographic evidence of degenerative joint disease. Calcification of the articular cartilage (of the femoral or tibial articular surface) was seen in 8 cases; involvement was bilateral in 7 of these. Here the characteristic appearance was that of a thin line of calcification parallel to the underlying bony articular surface (Fig. 3).

Meniscal calcification can usually be recognized by a Y-shaped radiodensity within the joint, just above the tibial plateau (Fig. 4, *A–D*). It is important to note that in the right knee of one case calcified menisci were seen in the tunnel view, but not in the routine anteroposterior projection; the calcified menisci in the left knee of the same case were seen in the routine anteroposterior roentgenogram but not in the tunnel view (Fig. 6, *A* and *B*; and 7, *A* and *B*). The importance of obtaining roentgenograms in both views when looking for calcified menisci is apparent.

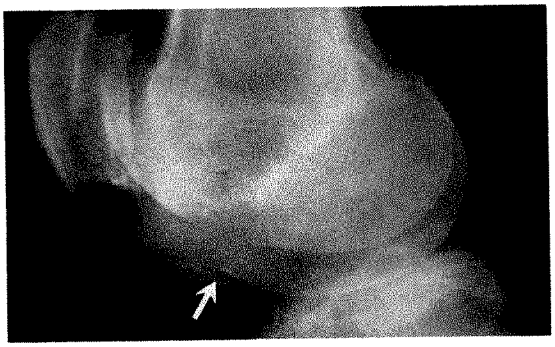


Fig. 3. Arrow points to articular cartilage calcification.

In summarizing the findings in the knee, it is evident that the most important sign is calcification of the menisci, usually bilateral, and readily visible in the tunnel view and/or the routine anteroposterior projection. Also important is the finding of calcification of articular cartilage in its superficial layer, most apparent in the lateral projection. Juxta-articular osteochondromata and "joint mice" are visible frequently, but their relationship to the other calcifications is unknown.

Calcification of the articular disk of the distal radioulnar joint was noted in 10 cases (of 18 with adequate roentgenograms); the process was bilateral in all cases but one (Fig. 8, *A–C*). Articular cartilage calcification of the wrist and carpal joints was often apparent, but was not seen in the absence of involvement of the articular disk.

Involvement of the symphysis pubis, manifested by a thin vertical line of calcification in its midportion, was seen in 8 cases (of 18 with adequate roentgenograms) (Fig. 9). A roentgenogram of a symphysis excised *en bloc* at necropsy shows that the calcifica-

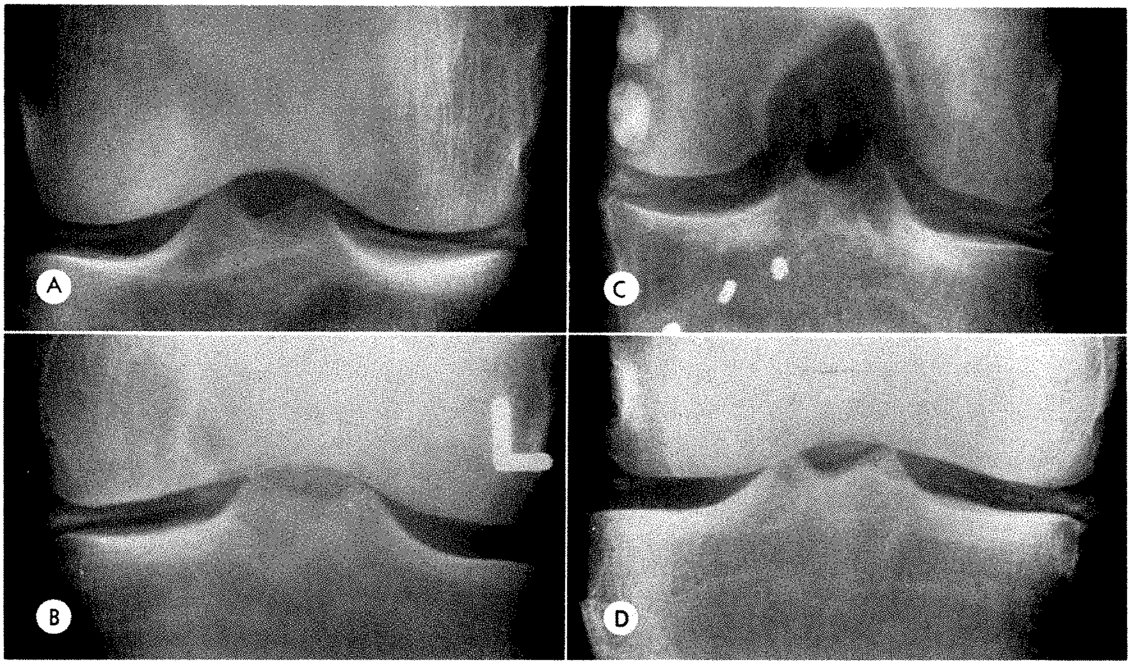


FIG. 4. (*A–D*) Typical appearance of calcified menisci.

tion occurs in a spotty, punctate fashion (Fig. 10).

Calcification of the annulus fibrosus was noted in 7 cases (Fig. 11). In all 7, there was symmetric involvement of the lumbar disks. In addition, 4 of these cases showed symmetric calcification of cervical disks and 2 showed involvement of thoracic disks. Almost all cases had roentgenologic evidence of mild to marked degenerative joint disease in the spine. Calcification of the nucleus pulposus, as seen in ochronosis, was not found. Of 18 cases with adequate roentgenograms, 9 showed calcification of the articular cartilage and/or capsule of the hip (Fig. 12); involvement was bilateral in 8 of the 9 cases. Moreover, the acetabular labrum often appeared to be calcified; this was the most heavily involved structure in the hips of 2 necropsied cases.

The shoulder was involved in 7 of 17 cases with adequate roentgenologic examination (Fig. 13); 4 of these showed unilateral calcification only. Again, the articular cartilage, joint capsule and glenoid labra were involved. Associated calcification in the supraspinatus tendon was seen in 5 cases. Calcification of the elbow was noted in 8 of 17 cases; in 6 cases involvement was unilateral. The capsule of the acromioclavicular joint was calcified in 3 cases, of a knuckle in 3 cases. One case (of 16 with adequate roentgenograms) showed bilateral calcification of the articular cartilage of the ankle.

Three cases showed mild unilateral sclerosis of the inferior aspect of a sacroiliac joint; however, no calcifications were seen in the joint itself. Ill-defined tendinous calcifications occurred not infrequently.

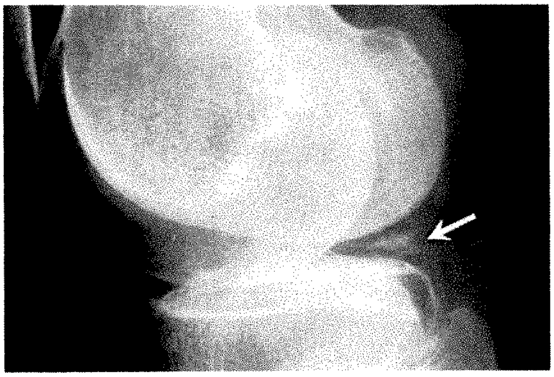


FIG. 5. Lateral view of calcified menisci.

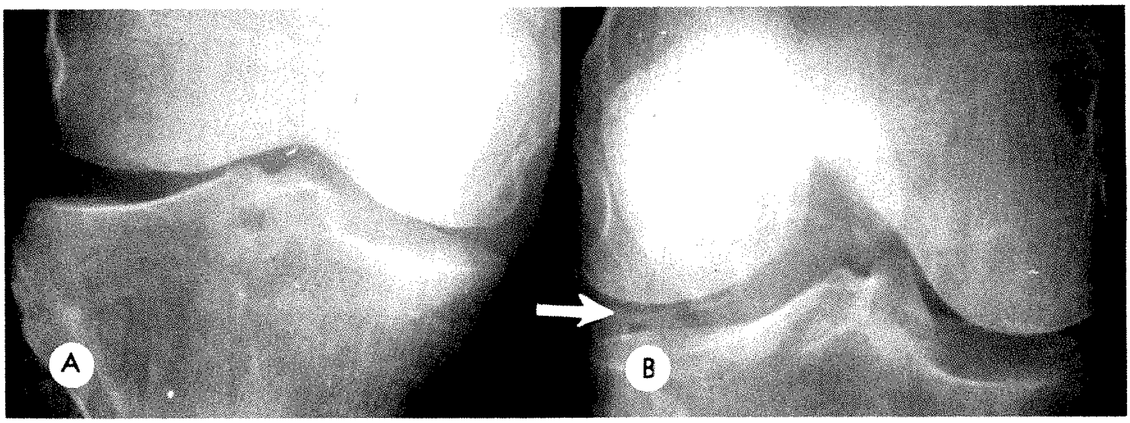


FIG. 6. (*A* and *B*) Meniscal calcification seen only in tunnel view.

Five cases showed extensive calcifications in the walls of muscular arteries (Mönckeberg sclerosis), one had associated Paget's disease of bone and one demonstrated bilateral calcifications in the ears. The relationship, if any, of the observations recorded in this paragraph to pseudogout is uncertain at the present time.

Figure 14 graphically summarizes the roentgenologic findings in 20 cases. It is apparent that the process tends to involve a given joint bilaterally and shows a propensity for fibrocartilaginous involvement. The menisci of the knee, articular disk of the distal radioulnar joint, symphysis pubis, annulus fibrosus of the intervertebral disks, glenoid and acetabular labra are frequently involved; all are fibrocartilaginous structures. The articular disks of the temporomandibular and sternoclavicular joints are also fibrocartilaginous, but were not studied systematically. Laminagraphy will be necessary in all probability to adequately demonstrate calcification in these areas. Articular (hyaline) cartilage is also involved frequently, particularly in the larger joints. Here again the process tends to be bilateral, although less so than is the case with fibrocartilage. Joint capsules are calcified not infrequently; judging from correlations of roentgenologic and necropsy findings, it is often difficult to tell roentgenographically whether a "rim" of calcification lies in articular cartilage, joint capsule or both.

DISCUSSION

The first description of meniscal calcification in the American literature was given in a case report by Israelski and Pollack[2] in

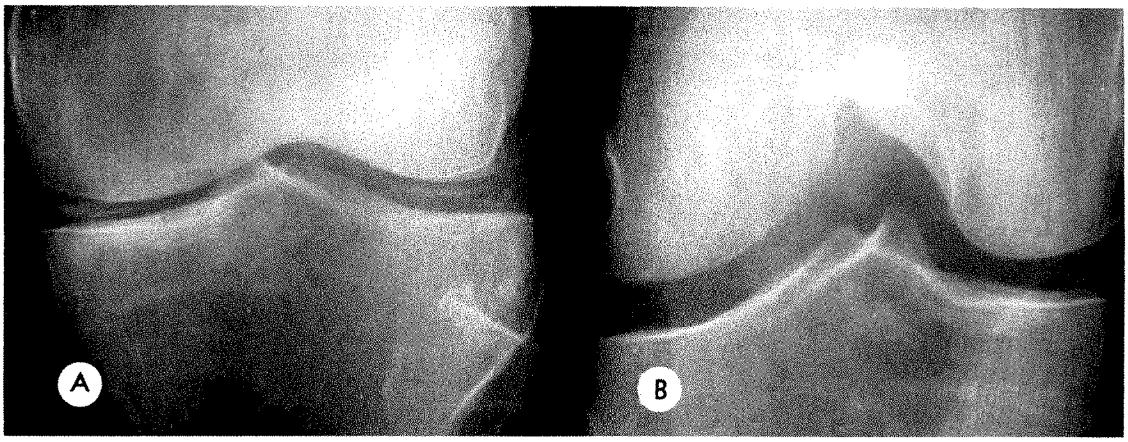


FIG. 7. (*A* and *B*) Meniscal calcification seen in routine anteroposterior view but not in tunnel view.

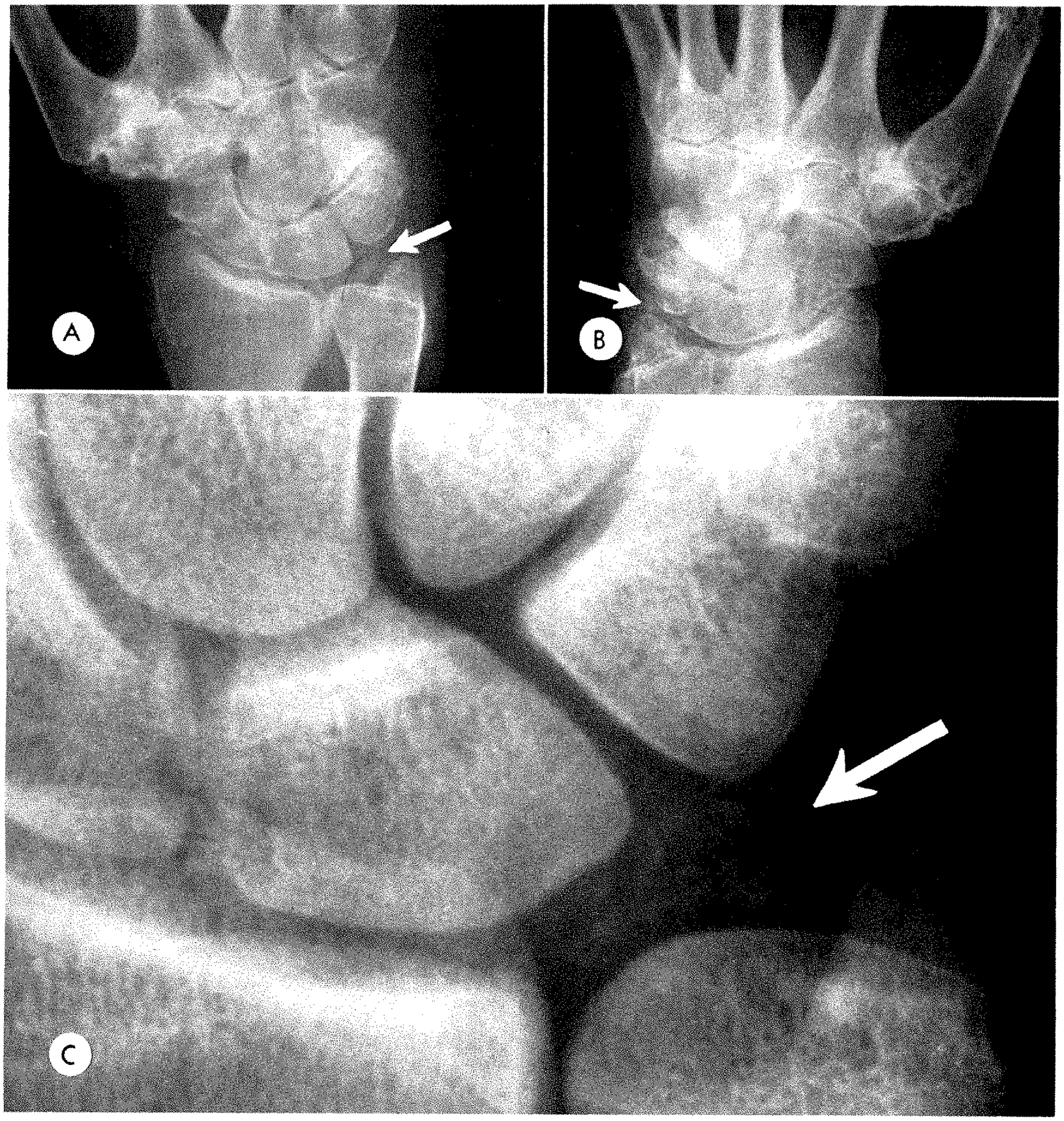


Fig. 8. (*A–C*) Calcification of the articular disk of the distal radioulnar joint.

1930. In the world literature up to that time only 6 cases had been recognized roentgenographically. All had onset of symptoms after the age of 45, were bilateral, and generally had no relation to trauma. Israelski and Pollack felt that the calcification was due to degeneration and necrosis of fibrocartilage.

In 1935, Wolke[9] described 8 cases of meniscal calcification among 2,569 roentgenologically examined knee joints (0.32 per cent). In several of his cases there were additional calcifications seen in the intervertebral disks and in the articular cartilage of various joints.

In 1942 Weaver[8] found a total of 76 cases in the world literature and reported an additional 2 cases. Only 43 of the 76 cases were felt to be of the primary or nontraumatic type. In these instances the calcium was laid down in parallel layers starting at the periphery and involving the entire meniscus. All but 4 of the patients were over 50 years of age; some had never had

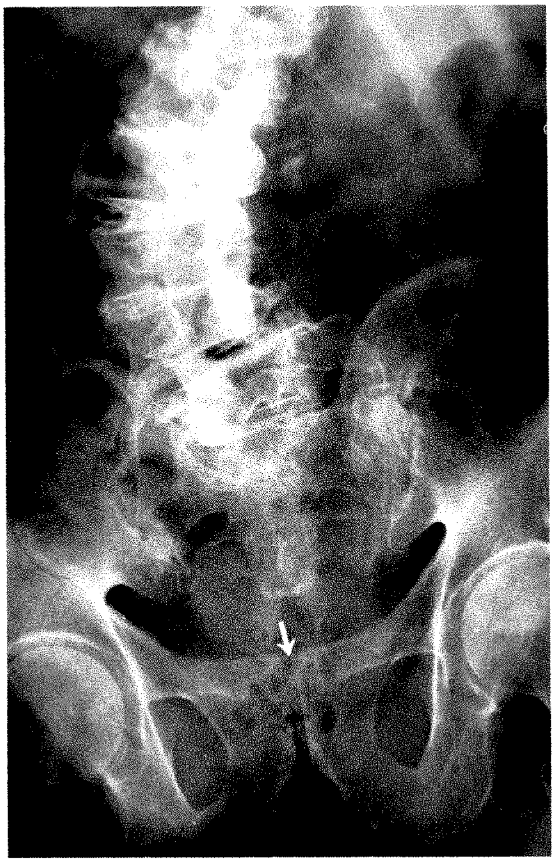


FIG. 9. Calcification of symphysis.

joint symptoms while others had recurrent attacks of pain, swelling and limitation of motion. A review of roentgenographic findings in the world literature at that time disclosed that 52 of 17,268 roentgenograms studied (0.42 per cent) showed calcifications.

The high incidence of roentgenographic involvement in this series is probably not a representative index of the true incidence of the condition because roentgen examination was used as a case-finding method.

Diagnostic Criteria. In order to better define this entity, certain diagnostic criteria are suggested; these are summarized in Table 1. These criteria are not intended as rigid dogma and will be modified or discarded as our knowledge of the condition increases. Use of the terms "definite," "probable" and "possible" is in good rheumatologic tradition.

As we have defined the condition by the presence of calcium pyrophosphate crystals, a "definite" diagnosis should include demonstration of the characteristic "fingerprint" of the crystal by x-ray diffraction powder pattern. The finding of nonurate crystals by polariscopic examination of a "wet" preparation of joint fluid or the presence of the characteristic roentgenologic findings makes the diagnosis "probable."

Roentgenographic findings which are felt to suggest a "probable" diagnosis are *bilateral* fibrocartilaginous or *bilateral* hyaline cartilage calcification. The occurrence of acute arthritis, especially of the knee or other large joint, with or without concomitant hyperuricemia, or of chronic arthritis

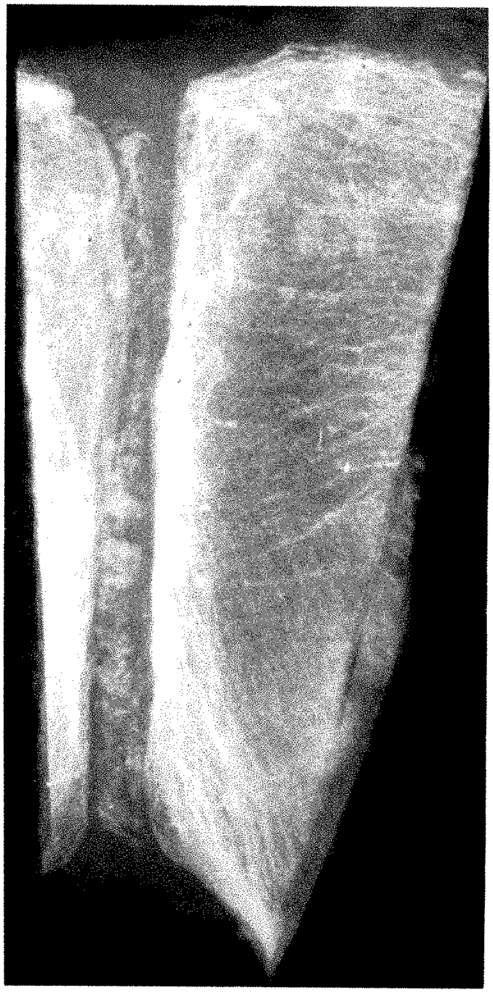


FIG. 10. Autopsy specimen showing articular cartilage calcification.

of large joints, especially if accompanied by acute exacerbations, should alert the clinician to the possibility of the condition. Only 13 of our 20 cases were "definite" by these criteria.

Projections which we have used routinely for screening purposes include: (1) anteroposterior, lateral, and tunnel view of both knees, (2) anteroposterior view of both wrists and hands on 1 roentgenogram, (3) anteroposterior view of the pelvis to see both hips, symphysis pubis and lower lumbar spine. If no calcifications are visible in these roentgenograms, it is highly unlikely that any will be visible in other areas.

Terminology. The condition described in this report has been called "pseudogout" because of certain resemblances to classic gout. The diagnosis of true gout was made outright or strongly entertained on clinical grounds in many of these cases by an observer who has had a particular interest in gout (DMcC). As our experience with the condition has grown and more cases have been discovered, it is apparent that the acute episodes in most cases of pseudogout do not resemble acute gouty arthritis if one anticipates the clinical picture of acute podagra. However, if one thinks of acute gout as an inflammatory host response to deposition of crystals in a vascular area (demonstrated recently in normal human and canine joints[1] and in the joints of gouty patients[7]) the analogy begins to formulate. Table II summarizes the similarities and differences by direct comparison.

Table I

DIAGNOSTIC CRITERIA FOR PSEUDOGOUT SYNDROME

Criteria

I. Demonstration of the characteristic "fingerprint" of the crystals of calcium pyrophosphate (obtained from biopsy, necropsy or aspirated joint fluid) by x-ray diffraction powder pattern

II. (a) Identification of nonurate crystals in synovial fluid (by polarized light microscopy)
  (b) Demonstration of bilaterally symmetric calcification of hyaline (articular) or fibrocartilage

III. (a) Acute arthritis, especially of knees or other large joints with or without concomitant hyperuricemia
  (b) Chronic arthritis, especially of knees or other large joints and if accompanied by intermittent acute exacerbations

Categories

A. Definite—Criteria I must be fulfilled

B. Probable—Criteria II (a) or II (b) must be fulfilled

C. Possible—Criteria III (a) or III (b) should alert the clinician to the possibility of the diagnosis

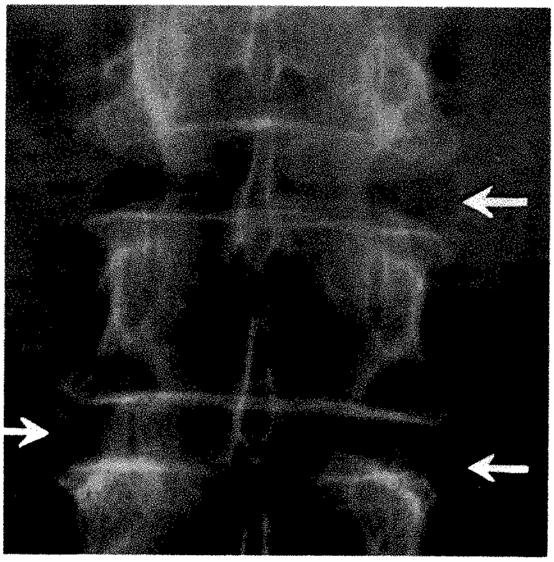


Fig. 11. Calcification of annulus fibrosus.

Most of the cases in this series were diagnosed as gout or as degenerative joint

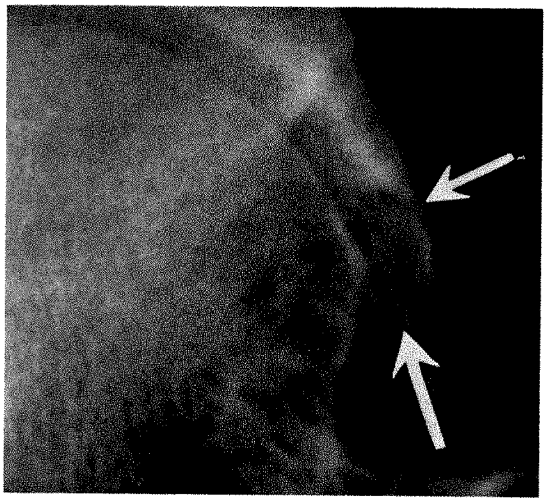


Fig. 12. Calcification in capsule of hip. Proven at autopsy.

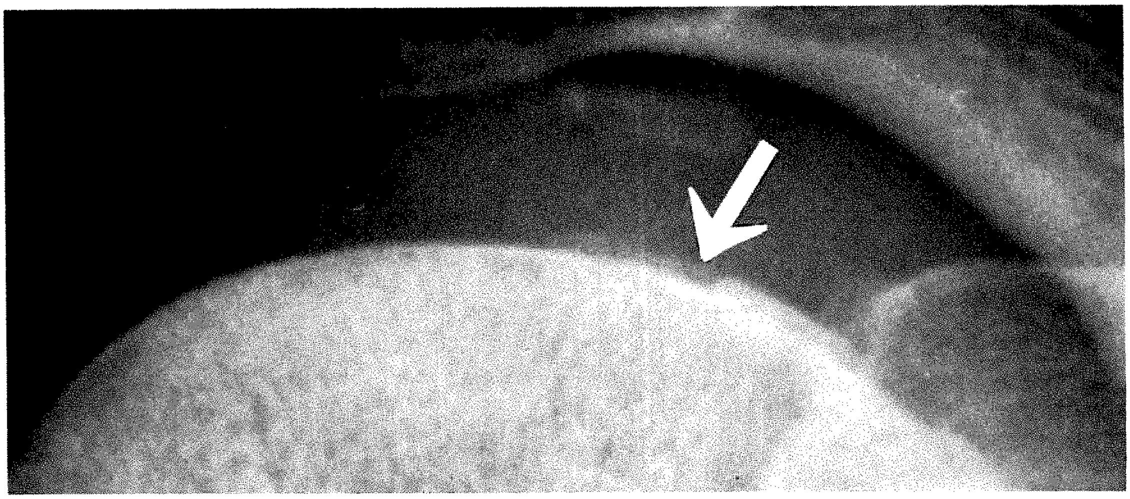


FIG. 13. Calcification of the articular cartilage of the humerus.

disease; a few were called rheumatoid arthritis. Careful clinical analysis in nearly every case, however, showed that the condition really resembles none of these completely. Indeed, one would not expect that it should; if it is a clinical entity, it should be able to stand on its own and be recognized for what it is. As a member of the arthritis family, it stands distinct from its siblings.

Until a more rational term, based on pathogenetic understanding, can be found, it appears reasonable to use a simple descriptive term to designate the condition. We have used the term "pseudogout" as this word-symbol.

TABLE II

COMPARISON OF SOME FEATURES OF THE SYNDROMES OF GOUT AND PSEUDOGOUT

Feature	Gout	Pseudogout
1. Male/Female	20/1	2–3/1
2. Acute attacks	present	present
(a) onset	sudden	sudden or gradual (over 24–48 hr.)
(b) duration	few days to few weeks	few days to few weeks
3. Joints involved	small joints mostly; bunion in 50 per cent; attacks	large joints mostly; never in great toe in this series
4. Colchicine response	often	unknown
5. Crystals present	yes; sodium urate	yes; calcium pyrophosphate
(a) intraleukocytic	yes; in acute attack	yes; in acute attack
(b) shape	rod (needle) shaped	rhombic and rod shaped
(c) size	0.5–20 microns	0.5–20 microns
6. Familial occurrence	yes; often	yes
7. Associated diseases	diabetes mellitus; hypertension; atherosclerosis	diabetes mellitus; hypertension; atherosclerosis
8. Chronic arthritis	yes; due to tophi in cartilage	yes; due to primary cartilage degeneration

SUMMARY

1. Pseudogout is a term coined to designate a type of arthritis associated with calcium pyrophosphate crystals in aspirated synovial fluid. These crystals are predominantly intraleukocytic in fluid from joints which are the site of an acute synovitis, and predominantly extracellular in fluid from chronically symptomatic joints. Injection of suspensions of these crystals into normal human or canine joints produced an acute inflammatory response.

2. The clinical, laboratory and roentgenologic findings in 20 cases of pseudogout are presented.

3. The calcifications seen on roentgenograms are composed of aggregates of microcrystals of calcium pyrophosphate, identical to those harvested from the synovial fluid.

4. Bilateral involvement of fibrocartilaginous structures is usually the most striking roentgenographic finding. The menisci of the knee, symphysis pubis, annulus fibrosus of the intervertebral disks, articular disk of the distal radiohumeral joint, glenoid and acetabular labra are often calcified. Articular cartilage, particularly of the large joints (knee, hip, shoulder and elbow), is also frequently involved. The roentgenographic appearance is characteristic and helpful diagnostically.

5. Diagnostic criteria for pseudogout syndrome are presented.

Daniel J. McCarty, Jr., M.D.
Department of Medicine
Hahnemann Medical College and
Hospital of Philadelphia
230 North Broad Street
Philadelphia 2, Pennsylvania

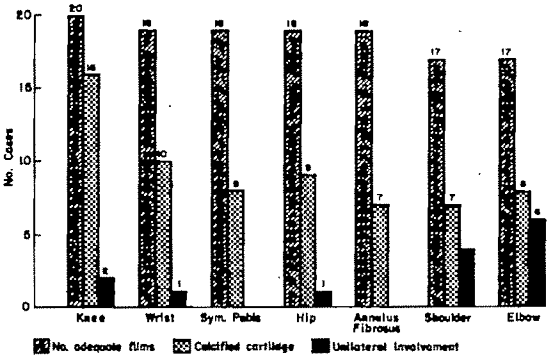


FIG. 14. Graphic summary of roentgenologic findings in the most commonly affected joints in 20 cases of pseudogout syndrome. These findings are quite characteristic and helpful diagnostically.

REFERENCES

1. FAIRES, J. S., and MCCARTY, D. J., JR. Acute arthritis in man and dog after intrasynovial injection of sodium urate crystals. *Lancet*, 1962, *2*, 682–684.
2. ISRAELSKI, M., and POLLACK, H. Über Kalkablagerungen in den Kniegelenken und Intervertebralscheiben. *Beitr. klin. Chir.*, 1930, *150*, 476–489.
3. KOHN, N. N., HUGHES, R. E., MCCARTY, D. J., JR., and FAIRES, J. S. Significance of calcium phosphate crystals in synovial fluid of arthritic patients: "pseudogout syndrome." II. Identification of crystals. *Ann. Int. Med.*, 1962, *56*, 738–745.
4. MCCARTY, D. J., JR., and GATTER, R. A. Pseudogout syndrome. III. Articular calcifications—occurrence, distribution, and identity with crystals found in synovial fluid. *Arth. & Rheum.*, 1962, *5*, 652.
5. MCCARTY, D. J., JR., KOHN, N. N., and FAIRES, J. S. Significance of calcium phosphate crystals in synovial fluid of arthritic patients: "pseudogout syndrome." I. Clinical aspects. *Ann. Int. Med.*, 1962, *56*, 711–737.
6. RAVAULT, P. P., VIGNON, G., LEJEUNE, E., MAITREPIERRE, J., and GAUTHIER, J. Diffuse articular chondrocalcinosis (à propos of 6 personal cases). *J. méd. Lyon*, 1961, *42*, 65–98.
7. SEEGMILLER, J. E., HOWELL, R. R., and MALAWISTA, S. E. Inflammatory reaction to sodium urate. *J.A.M.A.*, 1962, *180*, 469–475.
8. WEAVER, J. B. Calcification and ossification of menisci. *J. Bone & Joint Surg.*, 1942, *24*, 873–882.
9. WOLKE, K. Über Meniskus- und Gelenkknorpelverkalkungen. *Acta radiol.*, 1935, *16*, 577–588.
10. ZITNAN, D., and SITAJ, S. Chondrocalcinosis polyarticularis (familiaris); roentgenological and clinical analysis. *Cesk Rentgenol.*, 1960, *14*, 27–34.

STRESS FRACTURE WITH SPONDYLOLYSIS

By LEE A. HADLEY, M.D.
SYRACUSE, NEW YORK

SPONDYLOLYSIS, a break in continuity of the neural arch, either with or without spondylolisthesis, has already been thoroughly described and documented. In the patient here reported such a dehiscence developed as a result of unbalanced stress upon the fifth neural arch while he was under observation. Stress or fatigue fractures are not uncommon elsewhere. They may occur in normal bone subjected to a repetition of stresses, the cumulative effect of which exceeds the normal bearing capacity of that structure.[2,8] An example of this is the march fracture of the second, third and fourth metatarsals, the os calcis or the tibia which is frequently encountered, especially in untrained troops. Hartley[5] describes this condition as a "fatigue dystrophy," occurring during adolescence in normal bone and healing by callus formation when and if the stress is removed. Henschen[7] of Basel has studied by spectroradiographic methods the crystal derangements in the structures of bone under stress. Under these circumstances, "exhaustion fracture of the bone occurs if the rest period is inadequate," just as "fatigue" fractures develop in overstressed metals.

The "pseudofractures" of Milkman[10] or the "Umbauzonen" (rebuilding areas) of Looser[9] are somewhat similar. These also result from stresses, but they occur in pathologic states: osteomalacia, rickets, Paget's disease, etc. They heal slowly or remain unhealed as a band of uncalcified osteoid tissue having somewhat the appearance of a widened fracture line.[1] However, fractures of the isthmus or pars interarticularis do occur at times as the result of a single severe injury.[5]

The congenital theory of the origin of spondylolysis has not been substantiated and has been largely discarded by various students of the subject.[11,12] Rowe and Roche,[12] citing 509 examinations of spines in the newborn including their own series, were unable to discover any evidence of a congenital deficiency in the fifth neural arch. Neither was this author able to discover any evidence of a dehiscence crossing the pars interarticularis of the lower lumbar neural arches in the examination of 69 spines from stillborn infants. Spondylolisthesis may result from congenital lower lumbar anomalies, but these are distortions in the shape or length of the neural arch and need not be confused with the typical deficiency crossing the isthmus of the arch in about 5 per cent of all adults. In the newborn, each side of the neural arch is a spatula-shaped structure with a sturdy interarticular portion. As the child learns to walk and upon assuming the upright position, the formerly straight spine develops its lumbosacral angle, the isthmus elongates and becomes more slender and, most important of all, the area adapts itself to the low back shearing stresses of the human biped. From the shape of the arch in those individuals with spondylolysis, it is evident that the condition developed after the assumption of the upright position.

The tropho-static-dysplasia theory of origin of spondylolysis seems to be more strongly grounded.[11,13] Briefly, it explains this commonly encountered deficiency in the isthmus of the lowermost neural arch as resulting from a combination of shearing stress and atrition between the tips of the articular processes of the sacrum and the fourth lumbar vertebra. The pars interarticularis may become elongated and in certain cases the articular process tips exert pressure upon the slender intervening isthmus somewhat like the jaws of a pair of cutting pinchers.

REPORT OF A CASE

This male patient was first seen at the age of 14 years following a bicycle collision one month before. He had some pain at the left sacroiliac area, aggravated upon bending to the left but no other significant symptoms. Roentgenograms revealed six lumbar segments, the lowermost being sacralized on the left. The arch of this vertebra was somewhat elongated but appeared to be intact, as did the fifth neural arch on each side.

The patient returned 2 years later. Now, at the age of 16, the symptoms were more severe. He complained of low back pain especially on the left, aggravated by lateral bending. He stood with a list toward the left side and the lower lumbar area was obviously spastic. The Achilles and patellar reflexes were normal and referred pain was absent. Roentgenographic examination now revealed a well established spondylolysis of the fifth arch on the left (Fig. 1*B*). The tip of the superior articular process of the sacralized sixth segment was projecting upward into this dehiscence, while the inferior process of L4 articulated from above with the top of the deficient isthmus. Upon a restudy of the original roentgenogram, the fifth arch on the left was seen to be slender and possibly an infraction may have been present at the time of this examination (Fig. 1 *A*).

Of considerable interest, however, was the condition which had developed on the right side during the 2 year interval (Fig. 2*A*). Here, the pars interarticularis of L5 was now crossed by a band of decreased density quite similar to the pseudofractures of Milkman[10] or the rebuilding or transformation zones of Looser,[9] which occur at points of stress.

In retrospect, it appears that there was an original infraction, barely visualized, of L5 on the left in a slender isthmus. From this a definite, well established, spondylolysis resulted. Because of the unbalanced stresses thus created, this active boy developed a stress fracture in the previously normal fifth isthmus of the right side (Fig. 2 *B*).

Four years later it was found that the right inferior articular process of L4 had forced its way downward into the stress fracture, splitting open this defect. L5 had now descended so that its neural arch had eroded the tip of the right superior articular process of L6, and the articular surface of L5 now lay below and behind that structure. On the left side the condition was essentially unchanged except that L4 was slightly lower and the spaces at the dehiscence were smaller. At no time was there any spondylolisthesis. The patient did not develop a slipping, apparently because the isthmus of L5 on the right became hooked fast behind the articular process of L6. He did, however, develop a compensatory hypertrophy of the sacrospinalis muscles at this level. This is seen in Figure 3, a photograph of his back made at the time of the final examination. Symptoms were not severe at this time. Some discomfort was occasionally present following exposure to cold and dampness or after strenuous exercise such as water skiing. The patient, however, has developed into a vigorous 20 year old man without physical complaints or obvious disability.

DISCUSSION

Stress injury is a possibility to be considered in young people with backache, whose skeletal bony structure has not yet attained its ultimate strength.

Another patient of 19 years, reported by this writer, complained of increasing pain in the lower back. Roentgenograms showed a unilateral spondylolysis on the right side with minimal slipping only. This young man had developed a fracture through the pedicle of the opposite side. Subsequent examination 5 years later showed complete healing of the fracture of the left pedicle.[6]

Taillard,[18] in his excellent monograph on the spondylolisthesis, reports the case of a young woman who developed a stress fracture of the third neural arch. The strain at that point had resulted from a block fusion of the lumbar spine below that level at 15 years of age.

Hartley[6] described an "exhaustion" stress fracture of sudden onset involving a thoracic vertebra in a 17 year old boy. This youth had carried 100 pound bags of coal on his back during the past year. He had complained of some discomfort while at work. Later, and without any violence, there was sudden, acute dorsal pain and the patient was unable to sit up. The roentgenograms showed a collapsed wedge-shaped T5 vertebra with clean outlines. There was no evidence of pathologic change in the neighboring vertebrae. Further collapse occurred during the following week even while the

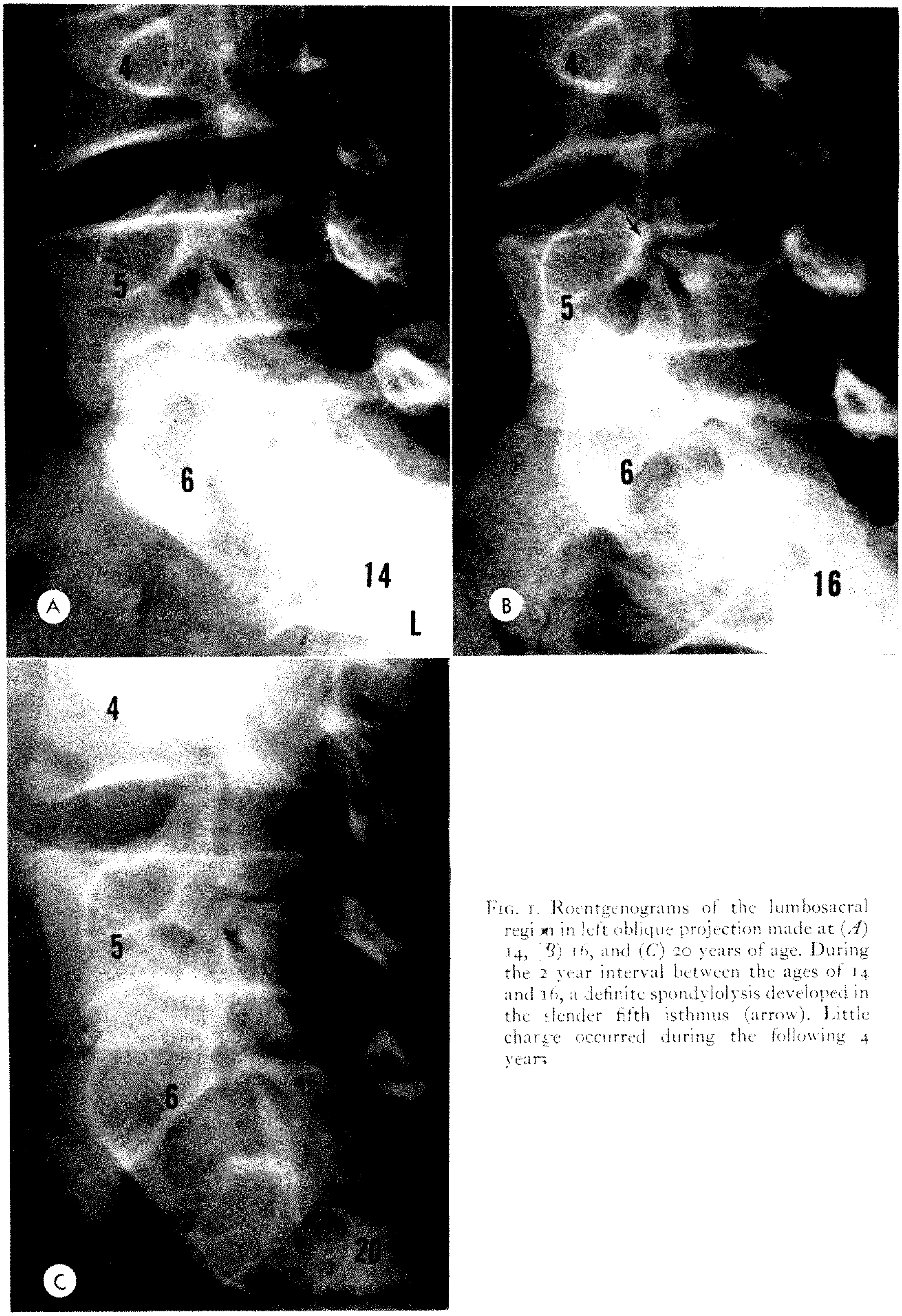


Fig. 1. Roentgenograms of the lumbosacral region in left oblique projection made at (*A*) 14, (*B*) 16, and (*C*) 20 years of age. During the 2 year interval between the ages of 14 and 16, a definite spondylolysis developed in the slender fifth isthmus (arrow). Little change occurred during the following 4 years.

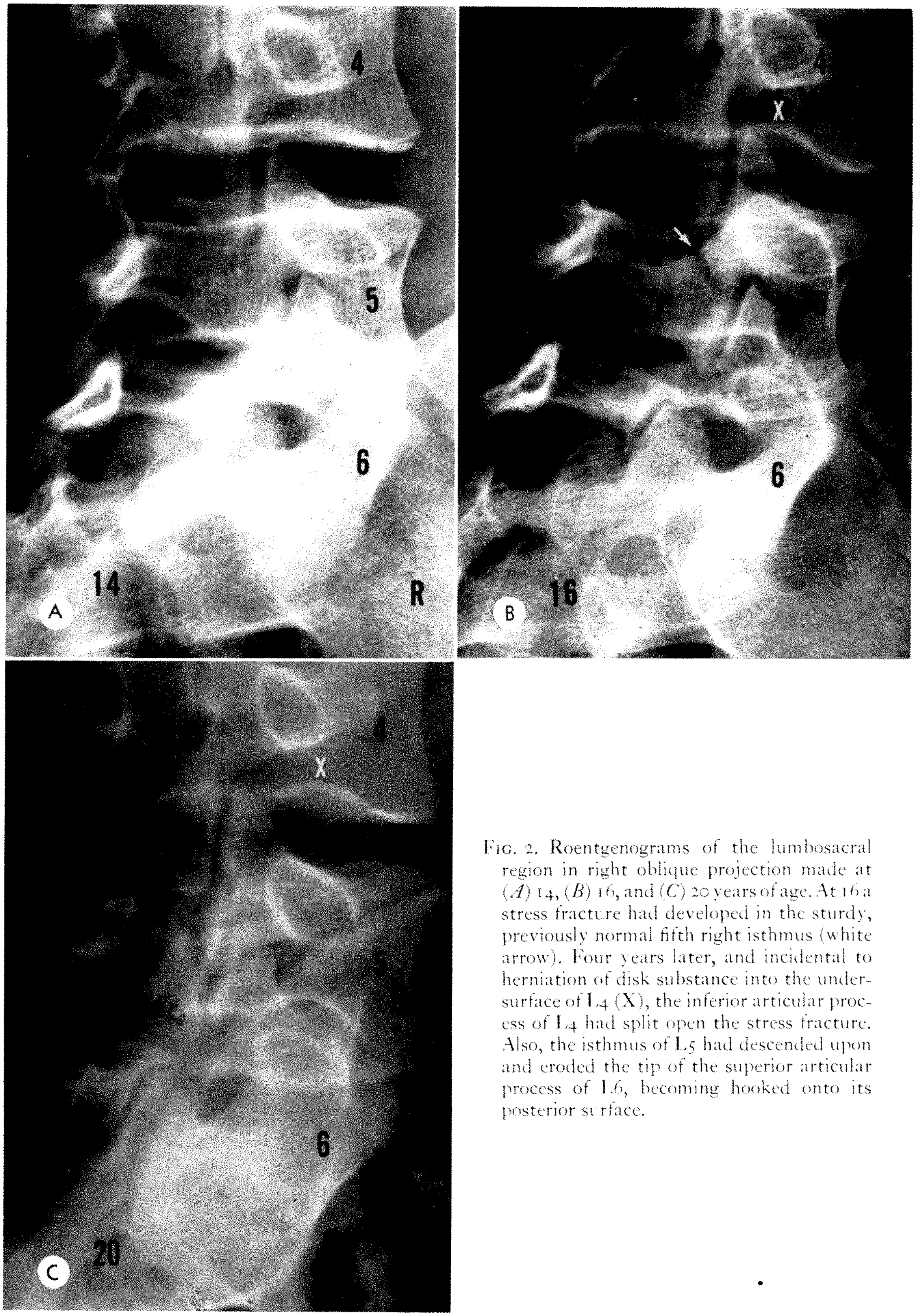


FIG. 2. Roentgenograms of the lumbosacral region in right oblique projection made at (*A*) 14, (*B*) 16, and (*C*) 20 years of age. At 16 a stress fracture had developed in the sturdy, previously normal fifth right isthmus (white arrow). Four years later, and incidental to herniation of disk substance into the undersurface of L4 (X), the inferior articular process of L4 had split open the stress fracture. Also, the isthmus of L5 had descended upon and eroded the tip of the superior articular process of L6, becoming hooked onto its posterior surface.

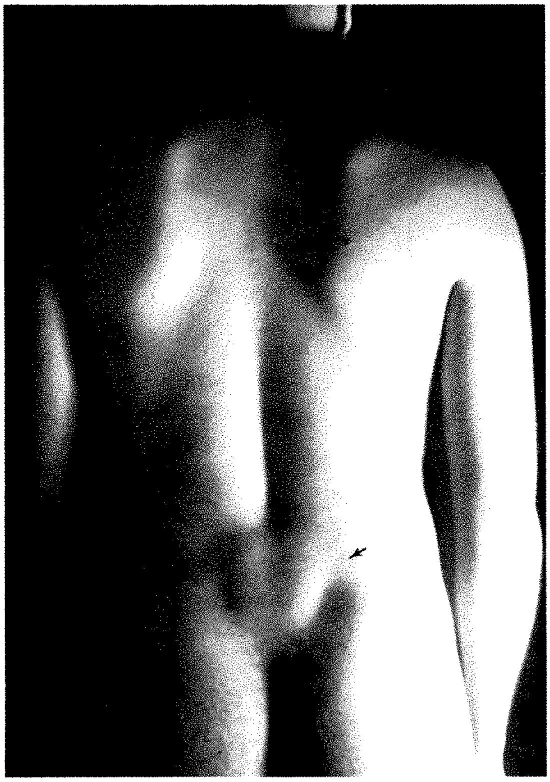


Fig. 3. Photograph of the patient's back at 20 years of age showing the compensating hypertrophy of the sacrospinalis muscles (arrow).

patient was resting in bed. Hartley considered this to be a fatigue fracture in a structure that had been subjected to excessive weight-bearing stress.

SUMMARY

A case is presented of a youth, studied from the age of 14 to 20 years, who developed a stress fracture in a normal fifth lumbar neural arch. This was caused by an unbalanced spondylolysis of the opposite side in a slender arch subjected to minimal trauma.

925 State Tower Building
Syracuse, New York

REFERENCES

1. Albright, F., and Reifenstein, E. C., Jr. Parathyroid Glands and Metabolic Bone Disease: Selected Studies. Williams & Wilkins Company, Baltimore, 1948.
2. Brandt, G. Creeping fractures (Transformation zones, overload injuries). *Ergebn. d. Chir. u. Orthop.*, 1941, *33*, 1–59. (Abstr. in Year Book of Radiology, 1941, p. 35.)
3. Hadley, L. A. Bony masses projecting into spinal canal opposite break in neural arch of fifth lumbar vertebra. *J. Bone & Joint Surg.*, 1955, *37A*, 787–797.
4. Hadley, L. A. Fatigue fracture of fifth lumbar neural arch. In: Clinical Orthopaedics. DePalma, A. F. *et al.*, Editors. J. B. Lippincott Company, Philadelphia, 1953.
5. Hartley, J. B. "Stress" or "fatigue" fractures of bone. *Brit. J. Radiol.*, 1943, *16*, 255–262.
6. Hartley, J. B. "Exhaustion" fracture of spine: preliminary report on one case. *Brit. J. Radiol.* 1943, *16*, 348–350.
7. Henschen, C. Quoted by Hartley[5] and Brandt.[2]
8. Krause, G. R., and Thompson, J. R., Jr. March fracture: analysis of two hundred cases. Am. J. Roentgenol. & Rad. Therapy, 1944, *52*, 281–290.
9. Looser, E. Über Spätrachitis und Osteomalacie. *Deutsche Ztschr. f. Chir.*, 1930, *152*, 210–357.
10. Milkman, L. A. Multiple spontaneous idiopathic symmetrical fractures. Am. J. Roentgenol. & Rad. Therapy, 1934, *32*, 622–634.
11. Nathan, H. Spondylolysis: its anatomy and mechanism of development. *J. Bone & Joint Surg.*, 1959, *41A*, 303–320.
12. Rowe, G. G., and Roche, M. B. Etiology of separate neural arch. *J. Bone & Joint Surg.*, 1953, *35A*, 102–110.
13. Taillard, W. Les Spondylolistheses. Masson & Cie, Paris, 1957. Die Spondylolisthesen (German translation). Hippokrates-Verlag, Stuttgart, 1957.
14. Wiltse, L. L. Etiology of spondylolisthesis. *J. Bone & Joint Surg.*, 1962, *44A*, 539–560.

VOL. 90, NO. 6

LUMBOSACRAL RETRODISPLACEMENT

By THEODORE A. WILLIS, M.D.
STANFORD, CALIFORNIA

SOME years ago there appeared in the same number of the *Journal of Bone and Joint Surgery* two reports of backward displacement of the fifth lumbar vertebra on the sacrum in which the diagnosis was based solely on the relation of the posterior border of the lumbar segment to the posterior border of the sacral segment.[2,5] Since the anterior borders of these centra appeared normally aligned, the present author measured the anteroposterior depth of the last lumbar and first sacral segments in 50 skeletons. In 33 of them the lumbar centrum exceeded that of the sacral in depth. For this reason such posterior displacements were called "optical illusions."[6] Believing then, as now, that any joint can be displaced if sufficient force is applied in the proper direction, this term should have been restricted to those displacements diagnosed only on the basis of the relation of these two vertebral borders.

Later authors recognized the difference in depth of the apposing vertebral surfaces but some, after deducting the discrepancy, maintained the same diagnositc criterion. So-called backward displacements were usually attributed to narrowing of the lumbosacral disk with consequent sliding downward and backward of the inferior articular processes of L5 on those of S1, which were thought to slope downward and backward.

In 1958, Melamed[3] found that in all of the sacra at his disposal the sacral articular processes extended downward, but not backward, in relation to their superior surfaces. The writer[7] confirmed this by the examination of 100 skeletons, in which a few were found with slight forward but none with backward inclination of the articular processes. There was also found frequent variation in length of the pedicles, proving that the posterior borders of the centra as shown on lateral roentgenograms are not dependable criteria as to the position of their articular processes. Melamed and Ansfield[4] felt that, because of frequent skeletal variations, the diagnosis of retrodisplacement necessitated more than an overlap of apposing posterior borders. They listed several other criteria necessary for such diagnosis.

Due to the angulation of the articular surfaces of the vertebrae from their sagittal planes and to their over-riding in the coronal planes, it is seldom, if ever, possible to demonstrate roentgenographically their relation to one another. In the study of the 100 skeletons, only one articular facet, a defective one, was found at right angles with its sagittal plane.[7]

In spite of this difficulty, there are still attempts to use this relation as a criterion of retrodisplacement. The hazards involved are well illustrated in Fletcher's[1] discussion of backward displacement. He made tracings of roentgenograms including the articular processes, then tracings to show the displacement properly reduced in which, after deducting the difference in depth of the centra, there was still an overhang of the lumbar border. It is noted in his tracings that in the displaced position there is an angle of 28 degrees between the inferior surface of the lumbar segment and the superior surface of the sacral segment, though their respective articular processes are parallel. In the "reduced" position the angle between the apposing body surfaces has been reduced to 18 degrees, but the processes are still parallel and are separated by the same distance as before. There is also a discrepancy in the distance between the posterior surface of the sacrum and its own articular process before and after reduction (Fig. 1 and 2).

What, then, does occur in those lumbosacral articulations that show, roentgenologically, marked narrowing of the lumbosacral disk and tipping backward of L5 on

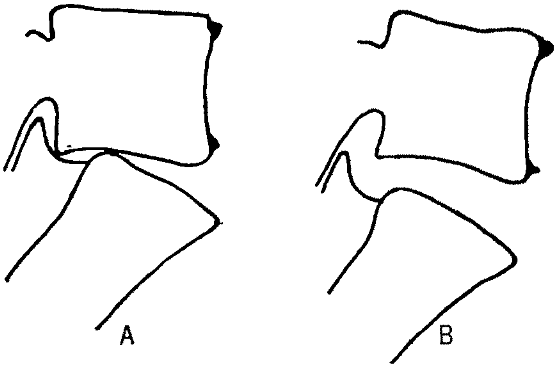


Fig. 1. Photograph of tracings of a lateral roentgenogram of the lumbosacral area showing retrodisplacement of the lumbar vertebra (*A*) in the displaced position and (*B*) in a "reduced" position. (Reproduced with permission of *J. Bone & Joint Surg.*[1])

S1 so that its inferior surface impinges on the posterior border of the latter (Fig. 3)?

Several years' search of dissecting room material has failed to disclose so extreme an example of retrodisplacement as some presented in reports of the problem. The one here presented is from the cadaver of an elderly male. The lumbar centrum is 3 mm. greater in depth than the first sacral. The disk is degenerated and bulges into the neural canal. The lumbar surface impinges on the posterior border of the sacrum. The lumbar articular facets extend one-third of their vertical length downward beyond those of the sacrum. They are rotated on the latter but not displaced backward. The sacral facets extend upward one-third of their length above the lumbar facets. The backward tilt of the lumbar segment increases the distance of the base of the lumbar processes from the sacral body (Fig. 4, 5 and 6). This position of hyperextension was made possible by the degeneration of the intervertebral disk. After maceration, the articular processes were found to extend downward at a right angle with the vertebral surfaces and at angles of 60 degrees with their sagittal planes.

Incidentally, in this pelvis the fifth lumbar nerve bundle was flattened over the pedicle of the sacrum. It was not pinched, as its foramen was several times the diameter of the bundle. A small branch from the flattened area extended dorsally. When the ligaments were stripped from the dorsum of the second sacral pedicle, a shell of bone was lifted, exposing a large cavity in the pedicle, filled with brown muck which, under the microscope, appeared to be blood cells distorted by the boiling procedure. The cavity measured 28×15×8 mm. It did not involve the centrum.

Whether this individual had had a backache, is not known, but there were present three possible sources for such a complaint: the degenerated bulging disk, the flattened nerve bundle and the sacral cyst.

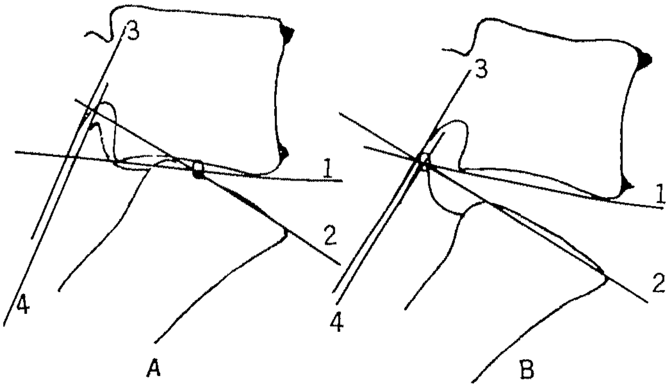


Fig. 2. Same as Figure 1, showing the angles of the vertebral surfaces and articular processes in relation to one another. In *A* the surface angle, 1-o-2, is 28 degrees. In *B*, the reduced position, the surface angle is 18 degrees. Though the lumbar centrum has been tilted 10 degrees, the articular processes have not. (Reproduced with permission of *J. Bone & Joint Surg.*[1])

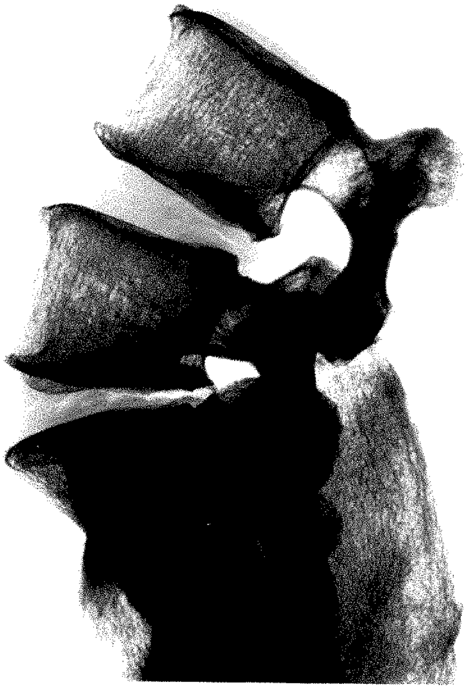


Fig. 3. A contact roentgenogram of a hemisection of the lumbosacral junction of the cadaver's column. Note the posterior overhang of the lumbar segment and its greater anteroposterior depth.

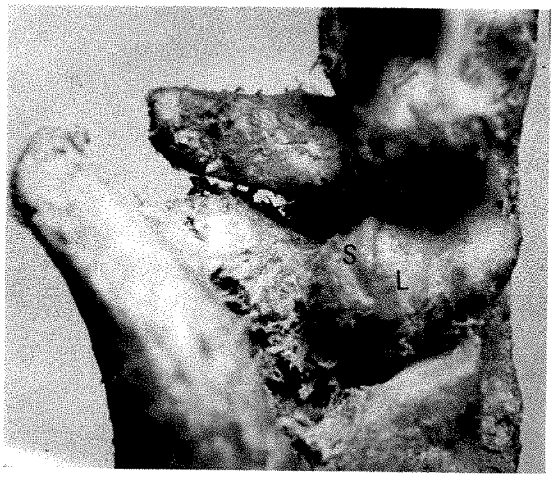


Fig. 5. Posterior view of the specimen. Note the downward extension of the lumbar facet on the sacral but no backward displacement.

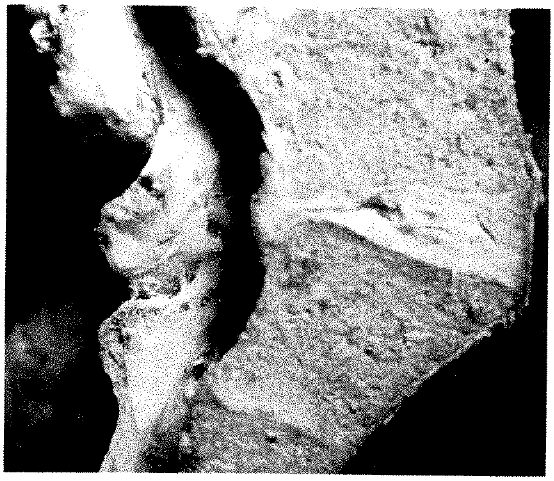


Fig. 4. Photograph of the sagittal section of the same specimen as shown in Figure 3. Note the degeneration and posterior bulging of the inter vertebral disk, the impingement of the inferior surface of L5 on the border of S1 and the difference in depth of the two centra.

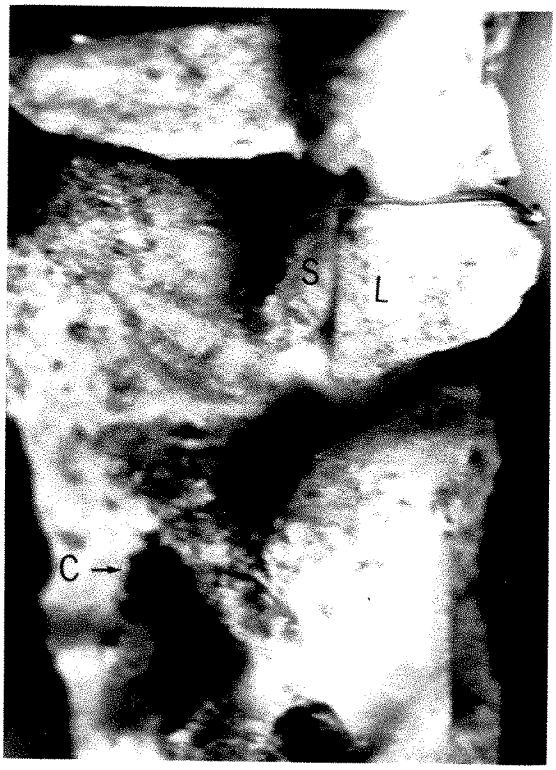


Fig. 6. Posterior view of the specimen with the macerated bones wired in their original positions. Note the relation of the articular facets, L and S, and the opening into a cyst, C̣, of the left lateral mass of the sacrum.

SUMMARY

An example of lumbosacral retrodisplacement in a cadaver is presented.

The need for more critical diagnostic criteria than the relation of the vertebral borders is emphasized.

Department of Anatomy
Stanford University
Stanford, California

1. Fletcher, G. H. Backward displacement of fifth lumbar vertebra in degenerative disc disease. *J. Bone & Joint Surg.*, 1947, *29*, 1019–1026.
2. Johnson, R. W., Jr. Posterior luxations of lumbosacral joint. *J. Bone & Joint Surg.*, 1934, *16*, 867–876.
3. Melamed, A. Some anatomical and roentgenologic considerations with respect to lumbosacral spine. *Radiology*, 1958, *71*, 548–551.
4. Melamed, A., and Ansfield, D. J. Posterior displacement of lumbar vertebrae; classification criteria for diagnosis of true retrodisplacement of lumbar vertebrae. Am. J. Roentgenol. & Rad. Therapy, 1947, *58*, 307–328.
5. Smith, A. DeF. Posterior displacement of fifth lumbar vertebra. *J. Bone & Joint Surg.*, 1934, *16*, 877–888.
6. Willis, T. A. Backward displacement of fifth lumbar vertebra: optical illusion. *J. Bone & Joint Surg.*, 1935, *17*, 347–352.
7. Willis, T. A. Lumbosacral anomalies. *J. Bone & Joint Surg.*, 1959, *41A*, 935–938.

VOL. 90, NO. 6

THE BRIM SIGN*

A NEW SIGN FOUND IN PAGET'S DISEASE (OSTEITIS DEFORMANS) OF THE PELVIS

By THOMAS R. MARSHALL, M.D., *and* J. T. LING, M.D.
LOUISVILLE, KENTUCKY

IN 1876 Sir James Paget described a disease process involving the bones and consisting of osteolysis followed by excessive reparative attempts which resulted in a weakened and deformed skeleton of increased bone mass. He called this "osteitis deformans." The familial occurrence of Paget's disease is occasionally seen. It is a condition of middle and old age, the average age of onset being between 50 and 55 years of age. Almost never is it found in persons under 35 years of age. It occurs more often in males by a ratio of 2 to 1.[1]

ETIOLOGY

The etiology is unknown and very little is known of the essential nature of the disease. Some feel that an excessive production of growth hormone at a late age may be responsible; others have suggested that an excessive intake of phosphorus may be a contributing factor.[5]

SITES OF INVOLVEMENT

The skeletal involvement in Paget's disease has a wide range of distribution; only one bone of the body (monostotic) or multiple bones (polyostotic) may be involved. Almost never are all of the bones of the body affected. The fibula is very rarely the site of the disease process. This fact is of value in the differential diagnosis. In our series of 550 patients it was involved in only 2 patients. Listed in order of their frequency of involvement are the pelvis, femur, skull, tibia, vertebrae, clavicles, humerus, and ribs. In our series the pelvis was involved in 50 per cent of the patients. The involvement is usually slowly progressive over a period of months and years. It starts in a small focus and gradually spreads to large areas of both cylindrical and flat bones. The serum calcium and phosphorus are usually normal since the disease is not primarily associated with calcium and phosphorus metabolism; however, with extensive skeletal involvement there is a hypercalcemia due to the destructive process in the bone. Serum alkaline phosphatase provides a measure of bone formation and serum hydroxyproline a measure of bone destruction. In some cases the serum alkaline phosphatase is very high, which is due to the excessive osteoblastic activity, and is proportional to the extent of skeletal involvement. The highest levels of serum alkaline phosphatase have been recorded in patients with extensive skeletal involvement.

STAGES

Paget's disease is divided into 3 types or stages (1) *destructive* (osteoclastic), (2) *mixed* (osteoclastic and osteoblastic), and (3) *sclerotic* (osteoblastic). Cyst-like areas may be present in all stages. The osteoclastic activity in the destructive phase leads to the increased vascularity of the bone and fibrosis. This is followed by the mixed stage with both osteoblastic and osteoclastic activity and new bone is laid down in some areas and destroyed in other areas. Histologically, there is a sharp demarcation between involved bone and the adjacent unaffected bone. This would seem to indicate that Paget's disease begins in a focal area and spreads peripherally until the entire bone has been involved. In the sclerotic stage, osteoblastic activity predominates. The bones become thickened and dense and the marrow cavities may be partially or completely obliterated.[4]

---

* From the Department of Radiology, University of Louisville School of Medicine, Louisville, Kentucky.

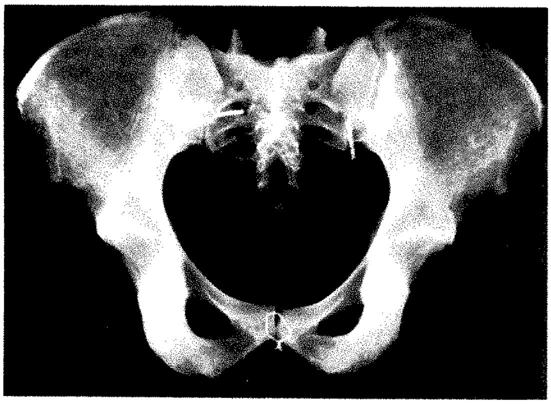


FIG. 1. Anteroposterior roentgenogram of the pelvic skeleton demonstrating the appearance of the pelvic brim (iliopectineal line).

The mosaic pattern in Paget's disease may be attributed to the irregular and curved cement lines within the bony tissues and the irregular notches and depressions on the surface of the spicules caused by the osteoclastic absorption. Histologic study shows a mosaic appearance with osteoclastic activity, eroding bone lamellae, and osteoblastic activity forming new bone. This new bone formation is interlaced with fibrous tissue. The characteristic haversian systems are partially destroyed and deformed and lose their orderly appearance. The medullary canal is largely replaced with fibrous tissue and cortical bone is replaced with spongy bone.[2]

THE BRIM SIGN

In our series of 550 patients with Paget's disease, 50 per cent had involvement of the pelvis. A study of these 225 patients led to the discovery of a new sign—the thickening of the pelvic brim or arcuate line (iliopectineal line). This is felt to be due to the added stress in this area because of the destruction of the lamellae in the pelvis and the resulting osteoblastic reaction, which occurs in Paget's disease. The ridge of bone around the pelvic brim, when osteoblastic reaction occurs, adds to the normal sclerotic density of this area. In an endeavor to increase the strength of the weakened bone, the trabeculae are formed predominantly in the lines of the greatest internal stress, and the normal bone trabeculae are exaggerated. A normal iliopectineal line is shown in Figure 1.

The brim sign was seen in 85 per cent of the cases of generalized involvement of the pelvis by Paget's disease in all stages (Fig. 2 and 3). It was of most value in distinguishing Paget's disease from metastatic carcinoma of the prostate when there was generalized involvement of the pelvis. The sign was found to be present even when there was unilateral involvement of the pelvis in the mixed and sclerotic stages of Paget's disease. It is, of course, not seen in the very early osteoblastic stage. Out of 250 patients with osteoblastic and osteolytic metastasis to the pelvis, it was seen in only one terminal patient with carcinoma of the prostate with almost pure osteoblastic metastasis to the pelvis. It was never seen in osteolytic metastasis to the pelvis or in the patients with mixed osteolytic and osteoblastic disease.

DISCUSSION

In the pelvis, one most frequently sees the combined phase of Paget's disease. The reparative process will keep up with the destructive process. Coarse trabeculation is

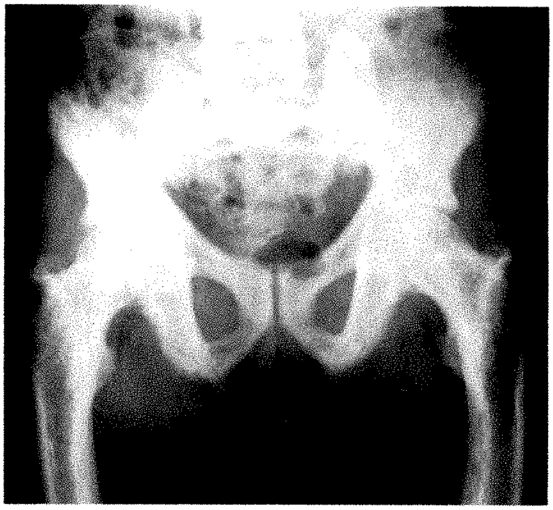


FIG. 2. A 65 year old male with proven Paget's disease. Roentgenogram shows the marked thickening of the iliopectineal line. Also note the widening of the pubic and ischial bones.

seen, and often this is first noted in the sacrum, where the bone structure develops a peculiar cross-hatched appearance.

Trabeculation of the ilium is usually more marked in the periphery, and increased trabeculae above the acetabulum are frequently an early finding. Widening of the bone is more frequent in the ischium and os pubis. Rarefaction is frequently quite prominent in the central portion of the ilia.

In the skull where there is no stress and strain, osteoclastic activity predominates even in early lesions. Due to the decreased resistance to pressure, the femoral heads often cause a heart-shaped deformity of the inlet of the lesser pelvis. Sclerosis of the pubic or ischial bones by osteoblastic metastasis usually does not lead to an increased diameter of the affected bones, except in the terminal stages. When widening of the bone occurs in osteoblastic metastasis, it is due to the infiltration of tumor cells beneath the periosteum and is more commonly seen in the ilium and superior pubic rami. This has the appearance of a wavy, irregular bone proliferation and does not resemble the widening seen in Paget's disease.

Osteoblastic metastasis is most often the result of carcinoma of the prostate. It is not common for carcinoma of the prostate to produce osteolytic metastasis. In osteolytic metastasis, there are solitary or multiple areas of bone destruction. These are usually circumscribed and there is no condensation of bone around the lesion in most instances (Fig. 4 and 5).

Carcinoma of the breast will occasionally produce osteoblastic metastasis to the pelvis, particularly when the tumor is slow growing and highly differentiated. Bronchogenic carcinoma, gastrointestinal carcinoma and vesical carcinoma also produce osteoblastic metastasis, but have not been

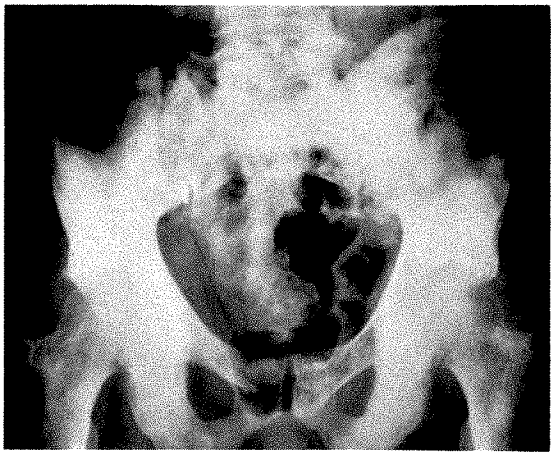


Fig. 4. Metastatic osteoblastic and osteolytic carcinoma of the prostate. Roentgenogram shows no evidence of thickening of the iliopectineal line.

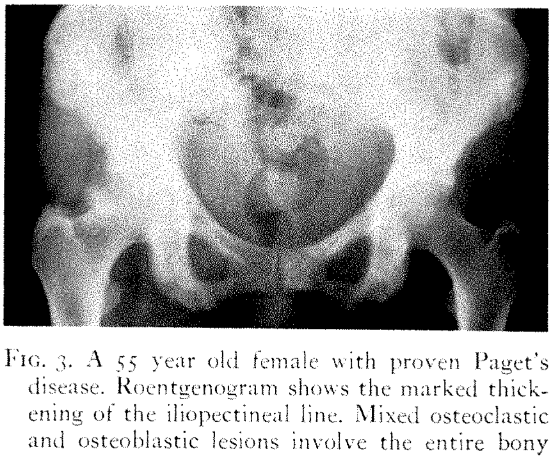


Fig. 3. A 55 year old female with proven Paget's disease. Roentgenogram shows the marked thickening of the iliopectineal line. Mixed osteoclastic and osteoblastic lesions involve the entire bony pelvis.

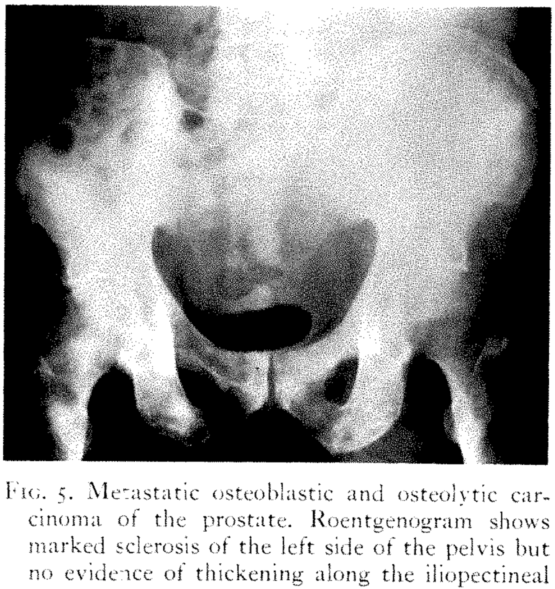


Fig. 5. Metastatic osteoblastic and osteolytic carcinoma of the prostate. Roentgenogram shows marked sclerosis of the left side of the pelvis but no evidence of thickening along the iliopectineal line.

known to produce thickening of the iliopectineal line (arcuate line).

In myelosclerosis, there is fairly uniform sclerosis of the pelvis which results from the formation of bony trabeculae in the fibrous tissue which has replaced the hematopoietic elements of the marrow. The trabeculae increase in number and this leads to a roentgenologic appearance of diffuse increased density of the bones of the skeleton. Osteoblastic metastasis is seldom as uniformly distributed as in myelofibrosis.

The incidence of sarcoma among 1,753 patients was 9 per cent. The average age of patients in whom sarcoma and Paget's disease co-existed was 58 years. The ratio of men to women among this group was 2 to 1. In order of frequency, the bones most commonly involved in cases of sarcoma with associated Paget's disease are the femur, humerus, pelvis, skull and tibia. Three of the 5 patients originally described by Paget developed osseous neoplasms.[3]

SUMMARY

A new sign called the "brim sign" is described which consists of thickening of the pelvic brim or arcuate line (iliopectineal line) in Paget's disease of the pelvis. This is felt to be due to the added stress in this area because of the destruction of the lamellae in the pelvis, and the resulting osteoblastic reaction which occurs in Paget's disease. The ridge of bone around the pelvic brim when osteoblastic reaction occurs adds to the normal sclerotic density of this area.

The sign is valuable in differentiating metastatic carcinoma of the prostate from Paget's disease. It was found in 85 per cent of the patients with Paget's disease of the pelvis in all stages, and even when there was unilateral involvement of the pelvis. It is rarely seen in metastatic osteoblastic metastasis and never in osteolytic metastasis to the pelvis.

T. R. Marshall, M. D.
Department of Radiology
University of Louisville
School of Medicine
323 E. Chestnut Street
Louisville 2, Kentucky

REFERENCES

1. Aegerter, E. E., and Kirkpatrick, J. A., Jr. Orthopedic Diseases; Physiology, Pathology, Radiology. W. B. Saunders Company, Philadelphia, 1958.
2. Anderson, W. A. D., Editor. Pathology. C. V. Mosby Company, St. Louis, 1948.
3. Porretta, C. A., Dahlin, D. C., and Janes, J. M. Sarcoma in Paget's disease of bone. *J. Bone & Joint Surg.*, 1957, *39-A*, 1314–1329.
4. Pugh, D. G. Roentgenologic Diagnosis of Diseases of Bones. Thomas Nelson & Sons, New York, 1951.
5. Snapper, I. Bone Diseases in Medical Practice. Grune & Stratton, New York, 1957.

PAGET'S DISEASE CONFINED TO ONE LUMBAR VERTEBRA

By MELVYN H. SCHREIBER, M.D., *and* GENE A. RICHARDSON, M.D.
GALVESTON, TEXAS

SINCE Paget's[6] first description of osteitis deformans in 1877, numerous cases of involvement of the nervous system, such as platybasia, optic atrophy, deafness, and trigeminal neuralgia as a result of destruction and distortion of the base of the skull, have been reported.[12] It was not until 1923, however, that the production of spinal cord symptoms by Paget's disease was reported by Wyllie,[15] who described 2 cases. In 1939 Schwarz and Reback[10] reported 9 cases of spinal cord compression, all apparently due to involvement of multiple vertebrae, and Turner[13] in 1940 added 7 cases with similar spinal cord compression due to involvement of multiple vertebrae. Dickson *et al.*,[2] analyzing 367 cases from the Mayo Clinic in 1945, reported neurologic evidence of compression of the spinal cord following pathologic fracture of vertebrae in only 6 cases. Exact sites of involvement were not stated, and it is not known whether or not polyostotic involvement was present. Rabiner and Hand[8] in 1947 reported 5 cases of Paget's disease which presented various types of symptomatology resulting from involvement of the nervous system. Two of these showed evidence of spinal cord compression, and in both there was involvement of multiple vertebrae as well as of other bones.

Extensive involvement of the thoracic and lumbar spine was described by Fairburn[3] in 1951, the patient requiring laminectomy from D3 to L3 inclusive for relief of symptoms. Latimer *et al.*[4] added 3 cases of multiple bone involvement with spinal cord compression in 1953 with localization at D5, D7, and D8 respectively, and after reviewing approximately 50 cases reported in the literature prior to 1953, concluded that all cases of spinal cord compression were of the polyostotic type.

In 1957 Ramamurthi and Visvanathan[9] described a case of Paget's disease confined to C2 causing quadriplegia; the spinal cord was compressed between the enlarged odontoid process and the body and lamina of the axis. Brailsford[1] in 1954 discussed Paget's disease in general and showed illustrations of a case in which the disease was confined to L3 without presenting neurologic symptoms and a case of multiple bone involvement with collapse of L3 and spinal cord compression.

Pugh[7] states that the sclerotic phase of Paget's disease involving the spinal column is most frequently seen when only one vertebral body is affected. The lesion seems to be uncommon, and neurologic involvement from Paget's disease of one lumbar vertebra must be quite rare. To our knowledge no such case has been reported in the medical literature. Because of this and because of the sparsity of reports of isolated Paget's disease in the radiologic literature,[1] we are prompted to report 3 cases, in one of which vertebral collapse produced neurologic symptoms requiring surgical decompression.

REPORT OF CASES

Case i. B.L.S., a 50 year old Caucasian male, was seen at The University of Texas Medical Center for psychotic depression, maxillary sinusitis, probable chronic cholecystitis, and suspected pancreatitis. Incidentally discovered during the course of his hospitalization was roentgenographic evidence of Paget's disease, isolated to the third lumbar vertebra (Fig. 1, *A* and *B*). The patient had no signs or symptoms which could be related to this roentgenographic finding. Alkaline phosphatase was 2.2 units and acid phosphatase was 0.75 units. No treatment was deemed necessary for the vertebral lesion.

Case ii. H.J.S., a 48 year old Caucasian male, complained of mild nonprogressive backache for many years, noted mostly on arising in the morning and relieved by exercise. All laboratory tests were within normal limits. Bone survey showed all bones to be normal except for Paget's disease of L3 (Fig. 2, *A* and *B*). This was first noted roentgenographically in 1954, and there has been little or no progression on roentgenograms to date. Symptomatic therapy was prescribed.

Case III. J.J.T., a 43 year old Caucasian male farmer, was admitted to the Neurological Division of the Department of Neuropsychiatry on January 8, 1957. He had a history of progressive weakness in the lower extremities for about one year, insidious in onset, resulting finally in complete foot drop bilaterally. There was no history of difficulty in bladder or anal sphincter control.

On physical examination the lower extremities were found to be thin in comparison with the upper, especially in the peripheral parts. The patient walked with a typical "steppage" gait with complete foot drop, being totally unable to dorsiflex either foot. Plantar flexion was also decreased in strength bilaterally. The right lower extremity showed slight generalized atrophy of the muscles including the gluteal region. Sensory examination revealed a very mild decrease in all sensations in the distal part of the right lower leg. There was no evidence of any disturbance in the saddle region. The deep tendon reflexes in the legs were active. Blood pressure was 110/70.

The electrocardiogram and electroencephalogram were within normal limits. Laboratory studies showed normal hemoglobin, white blood cell count, and differential. Acid and alkaline

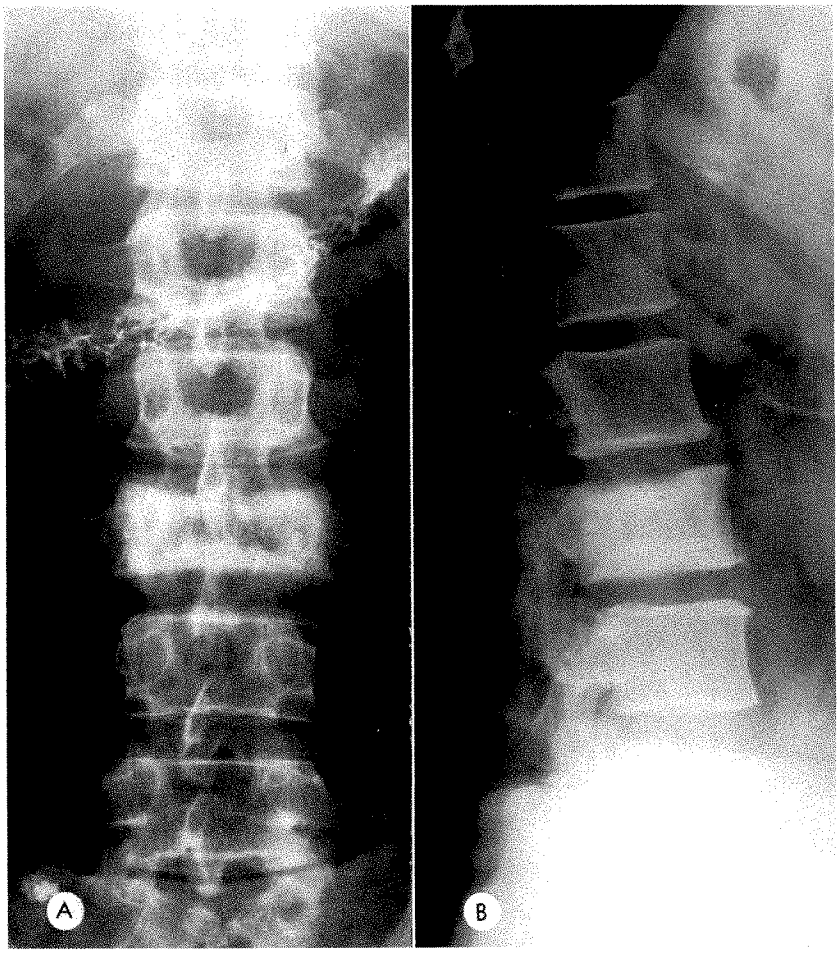


Fig. 1. Case I. Anteroposterior (*A*) and lateral (*B*) views of the lumbar spine show Paget's disease isolated to the third lumbar segment. The involved vertebra is increased in density, especially peripherally, and increased in anteroposterior and lateral dimensions. The internal trabecular structure is somewhat coarsened.

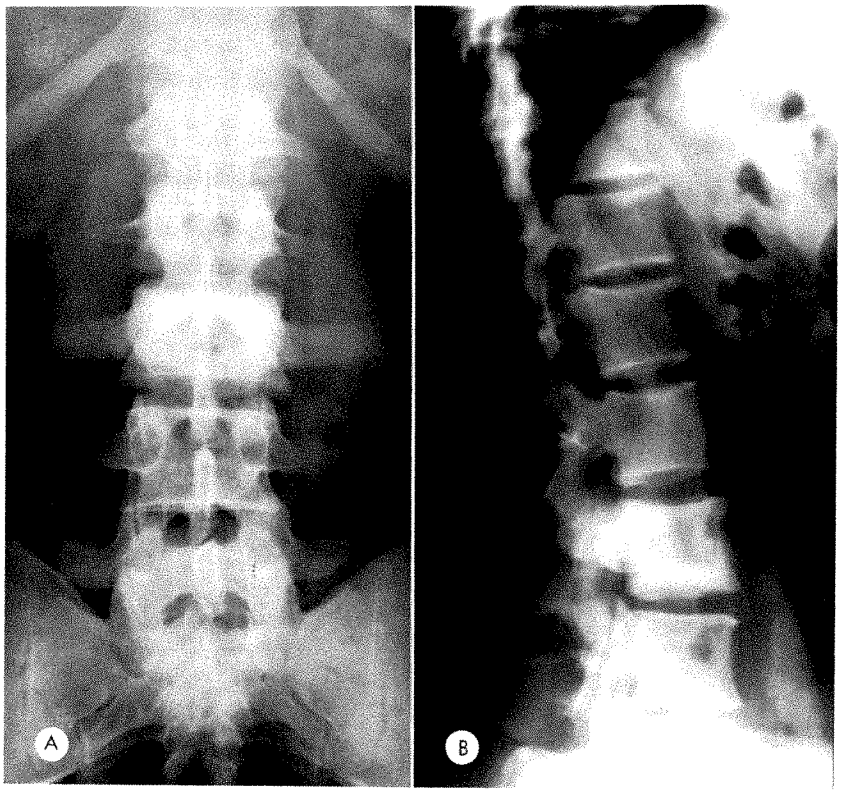


Fig. 2. Case ii. Anteroposterior (*A*) and lateral (*B*) views of the lumbar spine show increase in size and density of L3. The lateral view shows that the sclerosis is particularly marked peripherally. Paget's disease confined to the third lumbar vertebra.

phosphatase determinations were normal. The serologic test for syphilis was negative, and the urine analysis revealed no abnormality. Lumbar puncture showed no cells and 26 mg. per cent protein. The fasting blood sugar was normal.

Roentgenograms of the lumbar spine were obtained and lumbar myelography was performed. The lumbar spine studies demonstrated the body of the first lumbar vertebra to be widened both laterally and in the anteroposterior direction and flattened from above (Fig. 3, and 4, *A* and *B*). The superior and inferior vertebral plates were sclerotic, and the entire bone appeared more sclerotic than normal with a coarsened internal trabecular structure. No real destruction within the body of L1 was found, and it was noted that the transverse processes, the articular processes, the laminae, and the spinous process of L1 all appeared to be involved in the sclerotic process (Fig. 4, *A* and *B*). The myelogram showed a complete block of the lumbar subarachnoid space at the inferior level of the first lumbar vertebral body (Fig. 5, *A* and *B*).

The roentgenographic impression was complete block of the lumbar subarachnoid space at the first lumbar interspace, presumably due to compression at this level by the posterior extension of the enlarged body of L1. The possibility that these findings represented osteoblastic metastasis to the first lumbar vertebra was considered, but it was thought that isolated Paget's disease of L1 was at least as good a possibility. A skeletal survey showed no other bony lesion.

On digital examination the prostate was found to be normal in size and consistency. No nodules were palpated and no evidence of prostatic malignancy was thought to be present.

On January 16, 1957 the patient was operated upon. A laminectomy at the L1 level was performed, and the spinous process of L1 was noted to be grossly sclerotic. After the lamina was removed, bony compression of the dura by the overgrowth of L1 was seen. The laminectomy was completed with considerable difficulty, after which the dural sac appeared to be normal and pulsations were visible.

The pathologic specimen consisted of several

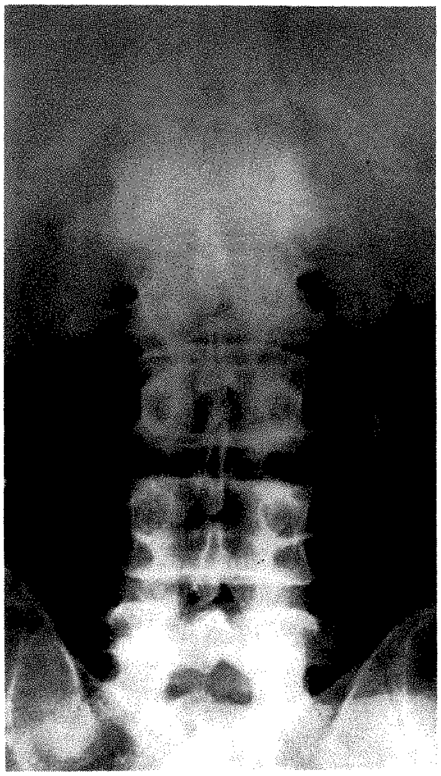


Fig. 3. Case III. Anteroposterior view of the lumbar spine showing isolated Paget's disease of L1.

small irregular fragments of bone and adjacent soft tissue. Microscopically, sections showed the histologic features of Paget's disease of bone. The bony trabeculae were seen to be markedly thickened and irregular in contour; they consisted of irregular plates of bone separated by blue cement lines. The nuclei of the osteophytes were intact, and there were moderate numbers of osteoblasts and osteoclasts at the irregular peripheral margins of these trabeculae. The structure was noted to form an irregular mosaic pattern, characteristic of Paget's disease. The marrow spaces contained loose fibrous connective tissue with a moderate number of vessels and a few marrow elements. There was no evidence of metastatic carcinoma and no evidence of sarcomatous transformation.

The patient recovered satisfactorily from the operative procedure and was discharged on January 24, 1957. He was seen in the Out-Patient Clinic on March 13, 1957, and was found to be much improved. No numbness, tingling, or pain was noted in the right leg and the patient's weakness had not increased. He said he felt stronger. On physical examination there was a definite foot drop on the right and only a slight foot drop on the left. The right leg muscles were slightly atrophic. The patient was seen again on August 6, 1962, by his local

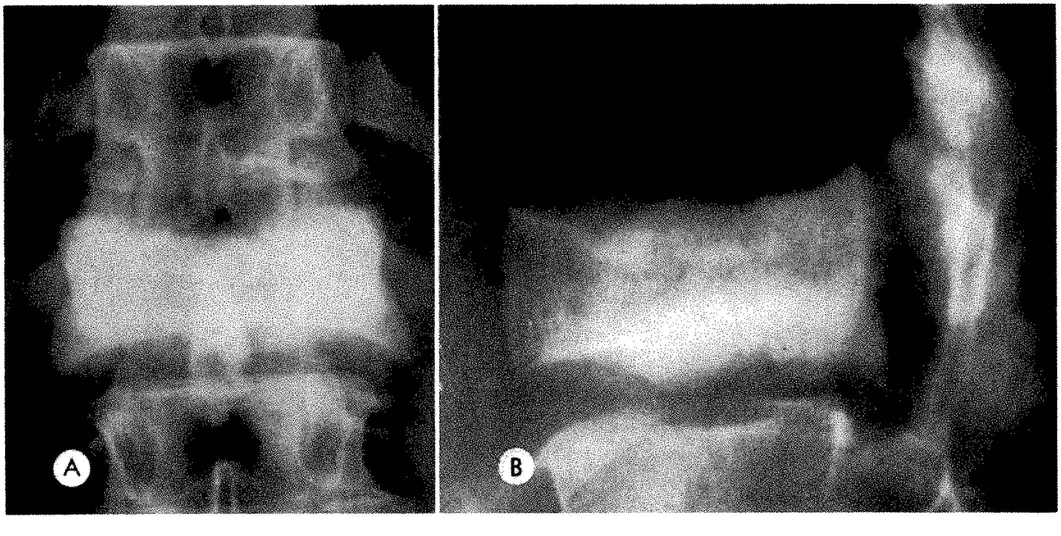


Fig. 4. Case III. Localized anteroposterior (*A*) and lateral (*B*) views of L1. The vertebral centrum is widened and flattened and increased in density. The lateral view shows considerable irregularity of the articular plates and posterior encroachment upon the vertebral canal by protrusion of the centrum. Particularly notable is the increase in size and density of the spinous process on the anteroposterior roentgenogram, indicating involvement of the neural arch as well.

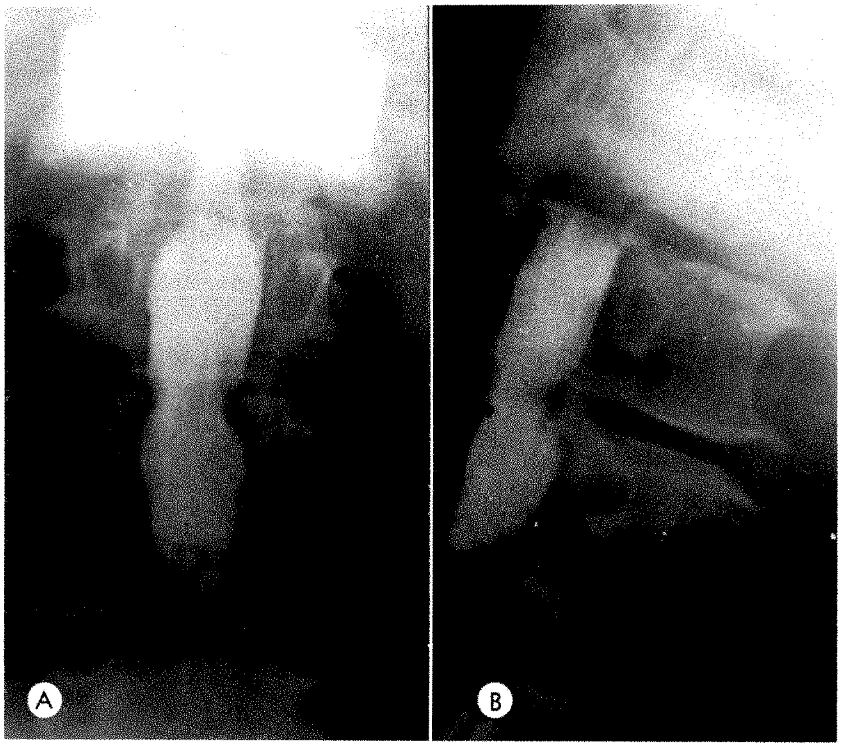


Fig. 5. Case III. Anteroposterior (*A*) and oblique (*B*) myelograms made with the patient in a steep Trendelenburg position. There is complete block of the lumbar subarachnoid space at the inferior margin of L1.

doctor and was thought to be doing very well. He still had considerable foot drop on the right and walked with the aid of a cane.

DISCUSSION

Spinal cord compression by a lesion in the vertebra is most often the result of traumatic injury, metastatic carcinoma, infiltrating sarcoma, tuberculous spondylitis, pyogenic osteomyelitis, osteoarthritis, infiltrating leukemia, or multiple myeloma.[12] Although osteitis deformans is not an uncommon disease and frequently involves the spine, it rarely causes compression of the spinal cord. The chief cause of such compression, when present, is a slowly progressive narrowing of the vertebral canal brought about by gradual enlargement of the diseased vertebral bodies and of the bone comprising the neural arches. Compression, collapse, or displacement of one or more of the softened vertebral bodies increases the mechanical distortion;[3] the bone may become markedly deformed by weight bearing, trauma or muscle action. Whalley[14] and Ramamurthi and Visvanathan[9] comment on the additional possibility of interference with the blood supply of the cord resulting in ischemia. Although sarcoma may develop in bones affected by Paget's disease, Porretta *et al.*,[6] reviewing the cases of sarcoma in Paget's disease at the Mayo Clinic up to 1956, found no spine lesions, and Sherman and Soong,[11] in 1954, reported 19 cases of osteogenic sarcoma in Paget's disease, in none of which was the spine involved. Whatever the specific morphologic abnormality responsible for the spinal cord compression, the treatment of choice is a decompression laminectomy.

The roentgenologic appearance of Paget's disease of the vertebra is rather characteristic. The centrum shows increased trabeculation, especially peripherally; the outline of the body is thus emphasized by roughly parallel exaggerated striations. The internal trabecular structure is coarsened, and the vertebra will often be increased in size and density. It may appear unusually square.

An important finding in our cases has been involvement of the entire vertebra, centrum, neural arch, and processes (Fig. 4, *A* and *B*). This appearance, plus the increase in size usually seen, helps to distinguish Paget's disease from osteoblastic metastases and hemangioma.

When compression fracture of the vertebra ensues, the roentgenographic picture is modified accordingly. The vertebral plates may be deformed and irregular, and the vertical dimension of the body will be decreased (Fig. 4, *A* and *B*). Posterior protrusion of the centrum with encroachment upon the neural canal may be obvious. Myelography may demonstrate complete or incomplete block at the affected level (Fig. 5, *A* and *B*). Lumbar puncture may show manometric block below the affected level and the spinal fluid protein may be elevated. In some cases lumbar puncture may fail, owing to the obliteration of the interlaminar spaces by a solid wall of new bone.[3]

The findings in isolated Paget's disease are in no way different from those described above except that the lesion is confined to one vertebral segment, there being no other roentgenologic evidence of osteitis deformans. Recognition of the characteristic findings and knowledge of the possible neurologic complications are important in distinguishing this entity from other vertebral lesions with which it may be confused, chiefly metastatic carcinoma and hemangioma.

SUMMARY

The literature on neurologic complications of Paget's disease of bone is reviewed and 3 cases of the lesion confined to one lumbar vertebra are reported. In one of the cases compression fracture of the involved vertebral body produced complete myelographic block and neurologic symptoms requiring laminectomy for decompression.

Melvyn H. Schreiber, M.D.
Department of Radiology
The University of Texas
Medical Branch
Galveston, Texas

REFERENCES

1. BRAILSFORD, J. F. Paget's disease of bone. *Brit. J. Radiol.*, 1954, *27*, 435–442.
2. DICKSON, D. D., CAMP, J. D., and GHORMLEY, R. K. Osteitis deformans: Paget's disease of bone. *Radiology*, 1945, *44*, 449–470.
3. FAIRBURN, B. Spinal cord compression in Paget's disease. *Arch. Middlesex Hosp.*, 1951, *1*, 190–197.
4. LATIMER, F. R., WEBSTER, J. E., and GURDJIAN, E. S. Osteitis deformans with spinal cord compression; report of three cases. *J. Neurosurg.*, 1953, *10*, 583–589.
5. PAGET, J. On form of chronic inflammation of bones (osteitis deformans). *Med.-Chir.*, 1877, *60*, 37–64.
6. PORRETTA, C. A., DAHLIN, D. C., and JANES, J. M. Sarcoma in Paget's disease of bone. *J. Bone & Joint Surg.*, 1957, *39A*, 1314–1329.
7. PUGH, D. G. Roentgenologic Diagnosis of Diseases of Bones. Williams & Wilkins Company, Baltimore, 1954, p. 423.
8. RABINER, A. M., and HAND, M. H. Paget's disease in central nervous system. *New York J. Med.*, 1947, *47*, 2689–2693.
9. RAMAMURTHI, B., and VISVANATHAN, G. S. Paget's disease of axis causing quadriplegia. *J. Neurosurg.*, 1957, *14*, 580–583.
10. SCHWARZ, G. A., and REBACK, S. Compression of spinal cord in osteitis deformans (Paget's disease) of vertebrae. AM. J. ROENTGENOL. & RAD. THERAPY, 1939, *42*, 345–366.
11. SHERMAN, R. S., and SOONG, K. Y. Roentgen study of osteogenic sarcoma developing in Paget's disease. *Radiology*, 1954, *63*, 48–58.
12. TENG, P., GROSS, S. W., and NEWMAN, C. M. Compression of spinal cord by osteitis deformans (Paget's disease), giant-cell tumor and polyostotic fibrous dysplasia (Albright's syndrome) of vertebrae: report of four cases. *J. Neurosurg.*, 1951, *8*, 482–493.
13. TURNER, J. W. A. Spinal complications of Paget's disease (osteitis deformans). *Brain*, 1940, *63*, 321–349.
14. WHALLEY, N. Paget's disease of atlas and axis. *J. Neurol., Neurosurg. & Psychiat.*, 1946, *9*, 84–86.
15. WYLLIE, W. G. Occurrence in osteitis deformans of lesions of central nervous system, with report of four cases. *Brain*, 1923, *46*, 336–351.

FRACTURE OF THE LATERAL PROCESS OF THE TALUS

By CHRISTIAN V. CIMMINO, M.D.*
FREDERICKSBURG, VIRGINIA

A PERPLEXING situation exists when pain defies specific diagnosis by either clinical or roentgenologic means and persists in an injured part. The purpose of this presentation is to call attention to the little known fracture of the lateral process of the talus, a cause for persisting disability if not diagnosed and treated.

Fractures of the talus comprise only about 1 per cent of all fractures; and fractures in the processes of the talus, especially the lateral, are even more unusual. Marótoli[3] collected 6 cases from the literature and added 4 of his own; Haage[2] also reported 1 case. The only reference in the English literature to this fracture appears in Dimon's article,[1] in which he reports 3 cases from the Fracture Clinic of the Massachusetts General Hospital, making a total of 14 cases.

We have seen such a fracture three times in 22 months at the Mary Washington Hospital which has 180 beds and a relatively active accident service; and we feel, therefore, that it is possibly more common than hitherto believed.

ANATOMY

The lateral process of the talus affords a surface for articulation with the fibula and for ligamentous attachments. The strong, short ligament between the tip of the lateral process and the subjacent calcaneus, the lateral talocalcaneal ligament, is of major interest as it regards the present fracture (Fig. 1). The surface immediately beneath the lateral process comprises a part of the posterior subtalar joint for articulation with the calcaneus.

MECHANISM OF FRACTURE

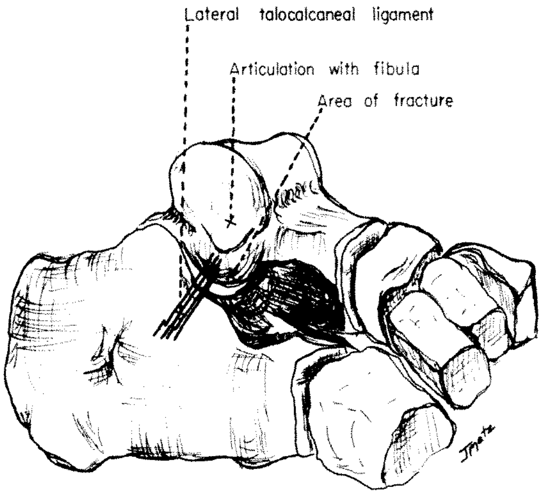


FIG. 1. The talocalcaneal region seen laterally and slightly anteriorly.

A fracture of the lateral process of the talus usually results from a vertical and forward fall such as occurs when unexpectedly stepping into a hole. Part of the lateral process becomes sheared by direct force from the subjacent calcaneus. It is also possible that forced supination of the foot could cause avulsion of the tip of the lateral process by the pull on the lateral talocalcaneal and other ligaments. A direct blow is a third possibility.

CLINICAL FEATURES AND TREATMENT

Immediate disability, with pain and swelling and later ecchymosis centered somewhat above and anterior to the tip of the lateral malleolus, occurs. The experience with this fracture is limited and therefore no definite treatment pattern is established but the following tentative scheme appears to be reasonable: (1) In patients with fresh, small, nondisplaced fractures, immobilization in a plaster cast for 1 month should be adequate; (2) in patients with

---

* Clinical Professor, Radiology, Medical College of Virginia.

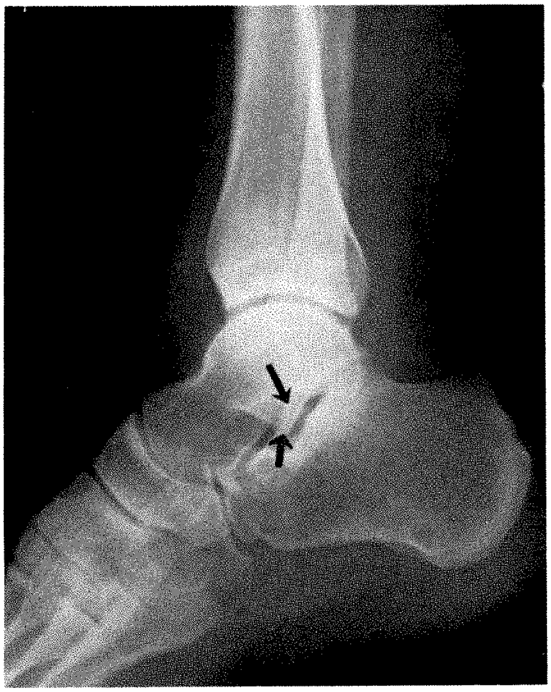


FIG. 2. A normal ankle. The upper arrow points to the apex of the upward directed sustentaculum tali and the lower arrow points to the downward directed apex of the lateral process of the talus. These structures must be identified.

fractures detected late, immobilization should be tried but eventual excision of the fragment may be necessary; and (3) in patients with fresh, displaced fractures, involving a significant portion of the posterior subtalar joint, immediate open reduction and internal fixation may be best.

Our 3 patients were all seen early, had small, nondisplaced fractures, and were subjected to conservative treatment. One is asymptomatic after 6 months, and the other 2 have been lost to follow-up.

Dimon's[1] experience would seem to indicate that this is not as benign a fracture as previously considered. All 3 of his cases were subjected to surgery: 2 had had initial immobilization that proved ineffective and continued to be symptomatic; the asymptomatic patient had had internal fixation of the displaced fragment as the primary treatment.

ROENTGEN FEATURES

The downward directed apex of the lateral process of the talus and the upward directed apex of the sustentaculum tali (the protuberance on the medial aspect of the calcaneus) are more or less superimposed on the lateral roentgenogram of the ankle (Fig. 2), even though they are on opposite sides. Identification of these two structures is necessary if fractures in either of these processes are to be recognized. Although not mentioned in the literature, soft tissue changes can be seen on the lateral roentgenograms. These are inflammatory infiltration into the calcaneal fat pad, and distention of tibiotalar and posterior subtalar synovial cavities with fluid. Posterior subtalar joint effusion should suggest this type of injury; however, its roentgenographic appearance is not widely known.[4]

The fracture is usually readily visualized on the anteroposterior roentgenogram of the ankle and a comparison with the lateral roentgenogram will exclude an accessory tarsal bone (Fig. 3; 4, *A* and *B*; and 5, *A* and *B*). In our 3 cases the oblique studies yielded no significant additional information.

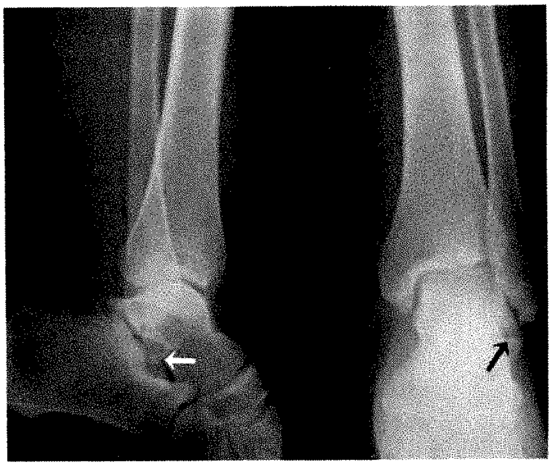


FIG. 3. Twenty year old woman injured in an automobile accident. The arrows indicate the fracture through the lateral process of the talus. Note on the lateral roentgenogram the additional fracture of the posterior process of the talus.

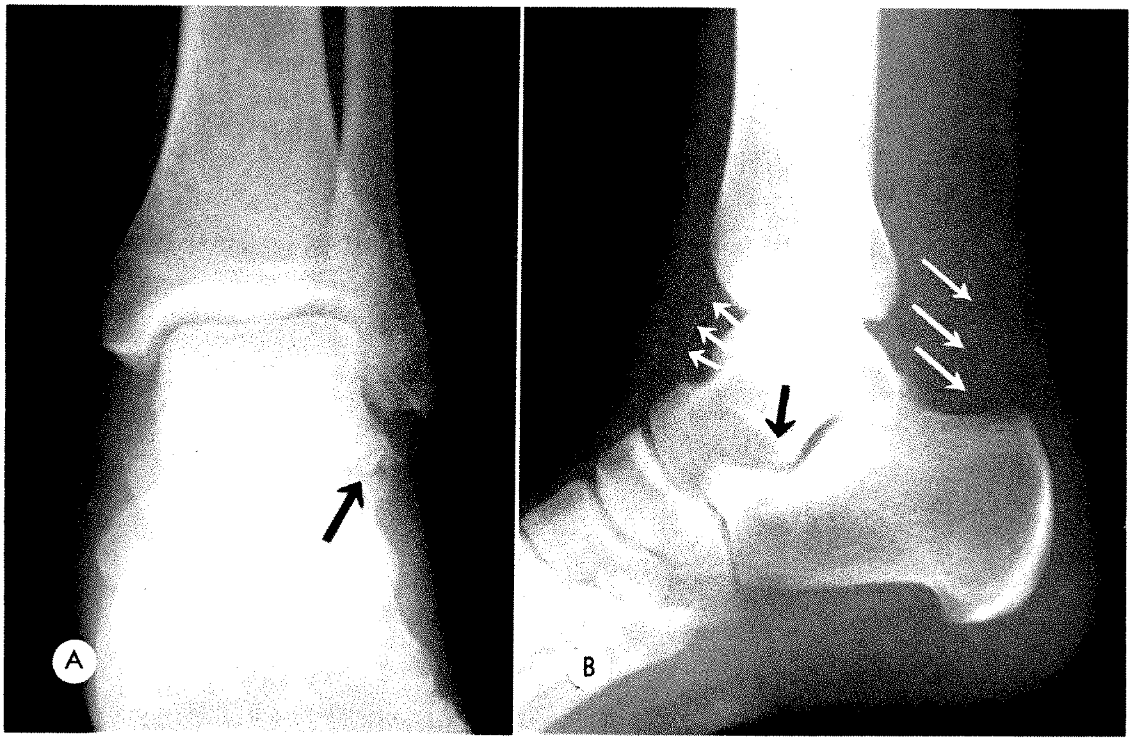


FIG. 4. Twenty-three year old man injured in an automobile accident. (*A*) Black arrow indicates fracture .(*B*) Anterior white arrows indicate ankle joint effusion. Posterior white arrows indicate inflammatory infiltration into the calcaneal fat pad. This probably hides the effusion in the posterior subtalar joint (see Fig. 5*B*)

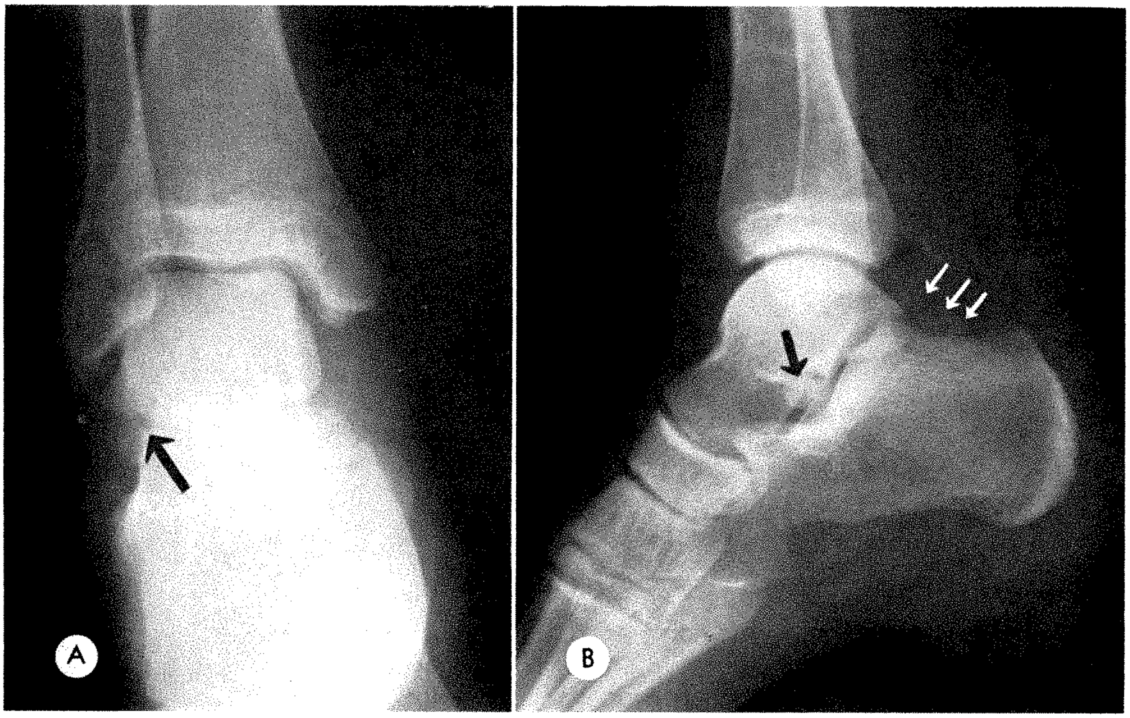


FIG. 5. Sixteen year old boy injured while playing basketball. (*A*) Black arrow indicates the fracture. (*B*) Posterior white arrows indicate posterior subtalar effusion with inflammatory infiltration into the calcaneal fat pad just above. This finding, especially in the absence of effusion into the ankle joint, should suggest this fracture.

A fracture of the lateral process of the talus can occur alone or with other fractures of the foot and ankle. For example, one of the previously reported cases and one of ours were associated with an avulsion of the posterior process of the talus; however, care should be taken in the interpretation of roentgenograms so that a congenital "ununited" process is not mistaken for a fracture.

SUMMARY

1. Fracture of the lateral process of the talus is probably not as rare as hitherto believed.

2. The fracture is caused by force directed to it through the calcaneus, by ligamentous avulsion, or by a direct blow.

3. Most patients respond well to immobilization for a period of 1 month. Some patients, especially those seen late, may require excision of the fragment. Immediate open reduction with internal fixation should be considered in those patients with fresh, displaced fractures of a significant part of the posterior subtalar articular surface.

4. A familiarity with the roentgenographic appearance of posterior subtalar joint effusion is recommended since its presence should suggest a fracture of the lateral process of the talus.

Department of Radiology
Mary Washington Hospital
Fredericksburg, Virginia

REFERENCES

1. DIMON, J. H., III. Isolated displaced fracture of posterior facet of talus. *J. Bone & Joint Surg.*, 1961, *43-A*, 275–281.
2. HAAGE, H. Isolierte Fraktur des Processus fibularis tali. *Forschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, 1961, *95*, 422–423.
3. MARÓTTOLI, O. R. Sobre las fracturas de la apófisis externa del astrágalo. *Rev. ortop. y traumatol.*, 1943, *13*, 107–117.
4. WESTON, W. J. Traumatic effusions of ankle and posterior subtaloid joints. *Brit. J. Radiol.*, 1958, *31*, 445–447.

VOL. 90, No. 6

CLINICAL EVALUATION OF CONRAY FOR ANGIOGRAPHY IN PATIENTS WITH CEREBROVASCULAR DISEASE*

By JORGE WEIBEL, M.D., WILLIAM S. FIELDS, M.D., E. STANLEY CRAWFORD, M.D.,
MICHAEL E. DEBAKEY, M.D., *and* ARTHUR C. BEALL, JR., M.D.
HOUSTON, TEXAS

SINCE Bernstein *et al.*[2] reported their experimental studies with angio-conray as contrast material for angiography, several other authors[1,3,5,6,8,9] have reported their clinical experiences using angio-conray 80 per cent and conray 60 per cent for intravenous pyelography, direct and retrograde aortography, and cerebral and other peripheral arteriography. Conray and angio-conray are highly water-soluble, low viscosity, organic iodide contrast agents manufactured by the Mallinckrodt Chemical Works, St. Louis, Missouri. The generic name for the free acid is iothalamic acid, which contains 62 per cent iodine. The product is available in two forms: (1) a solution of meglumine iothalamate 60 per cent, containing 28 per cent iodine (conray), and (2) a sodium iothalamate solution 80 per cent, containing 48 per cent iodine (angio-conray). This new contrast material appears to be well tolerated, and the results obtained from the studies made have been highly satisfactory. No major complications have been reported in any of the published papers, and only minimal and transient side effects have been observed.

Until July, 1962, we employed sodium diatrizoate 50 per cent (hypaque*) for arteriographic study in patients having cerebrovascular insufficiency and other types of lesions involving the intracranial structures. Although sodium diatrizoate 50 per cent provided satisfactory arteriographic visualization of all kinds of abnormalities, the side effects were more marked than those which occur when using conray, particularly when the angiographic procedure is performed under local anesthesia. With sodium diatrizoate 50 per cent, convulsions, nausea, vomiting, hypotension, flushing, and cutaneous manifestations of allergic type have occurred with some frequency. One of the most undesirable side effects of sodium diatrizoate 50 per cent is the painful burning sensation experienced by most patients,[7] especially when the subclavian artery is injected. This burning sensation will occur even though the injection is carried out by means of catheterization. Although this disadvantage may obviously be disregarded when general anesthesia is used, it is difficult to obtain the patient's cooperation when several injections must be performed under local anesthesia.

In August, 1962, we began clinical evaluation of conray 60 per cent for use in angiographic diagnosis of vascular lesions in patients suffering from cerebrovascular insufficiency. Our experience with this contrast material in such patients and also in some cases of intracerebral disease other than vascular is reported herein.

CLINICAL MATERIAL

The results in 192 patients admitted for arteriographic study to the Methodist Hospital, Houston, Texas, since August, 1962, were reviewed. Their ages ranged between 22 and 80 years (76 per cent over 50 years); 130 were male and 62 female. One hundred and sixty-four patients were

* Winthrop Laboratories, New York, N. Y.

---

* From the Department of Neurology and the Cora and Webb Mading Department of Surgery, Baylor University College of Medicine, Texas Medical Center, Houston, Texas.

This work was supported in part by Grants HE-04763 and HP-5435 from the National Heart Institute, National Institutes of Health, United States Public Health Service.

TABLE I

GROUP A: DIRECT PUNCTURE OF THE SUBCLAVIAN AND CAROTID ARTERIES

	No. of Cases
Bilateral subclavian	20
Bilateral carotid and left subclavian	2
Bilateral carotid and right subclavian	1
Bilateral carotid	26
Right carotid	4
Left carotid	1
Total	54

admitted with the diagnosis of cerebrovascular insufficiency and 28 with cerebral disease other than circulatory disturbance. In all patients in this series, conray 60 per cent only was used. No single injection exceeded 30 ml., and the total amount injected at one session varied between 10 and 240 ml.

METHOD AND TECHNIQUE

Direct percutaneous infraclavicular catheterization or direct supra- and/or infraclavicular percutaneous puncture of the subclavian arteries was employed in this series.[4,10,11] Whereas catheterization of the right subclavian artery was employed for visualization of the right carotid system, the left common carotid artery was injected directly. Bilateral direct carotid arteriography was carried out for the purpose of obtaining serial roentgenograms for visualization of the arterial and venous phases of the cerebral circulation. Whenever we failed to visualize the right common and internal carotid arteries by indirect injection of the innominate artery by means of catheterization of the right subclavian artery, the right common carotid was also punctured directly. In those cases in which the subclavian arteries were punctured percutaneously through the supra- and/or infraclavicular approaches, the right and left internal carotid arteries were visualized by direct puncture of the common carotid arteries. In some cases only one or two arteries were injected, using one or both procedures. The number of patients and the arteries injected are summarized in two groups: A and B (Table I and II).

Direct puncture of the subclavian artery through the supra- or infraclavicular approaches provides, in most cases, satisfactory filling of the origin and cervical course of the vertebral artery and, in a few cases, visualization of the innominate, right common, and internal carotid arteries. However, this procedure does not always permit satisfactory visualization of the basilar artery and its branches, and in some cases local artifacts, intramural injections, extravasation of contrast material, and pneumothorax may occur. For this reason, we have preferred catheterization of the subclavian arteries through an infraclavicular puncture. This method, in our experience, provides very satisfactory visualization of the extra- and intracranial vessels which supply the brain, and also permits us to perform selective filling of a single artery, when necessary, or visualization of several large vessels by a single manual injection.

In Group B, the right common and internal carotid arteries were satisfactorily visualized in 111 out of 128 patients in whom the right subclavian artery was catheterized. In 68 patients the left common carotid artery was visualized by injection through a catheter placed at the level of the origin of the innominate artery, and

TABLE II

GROUP B: CATHETERIZATION OF THE SUBCLAVIAN ARTERY AND DIRECT INJECTION OF THE CAROTID ARTERY

	No. of Cases
Bilateral subclavian catheterization	128
Bilateral direct carotid injection and left subclavian catheterization	6
Bilateral direct carotid injection and right subclavian catheterization	2
Right subclavian catheterization and left direct carotid injection	1
Left subclavian catheterization only	1
Total	138

in a few of these same patients all large vessels having their origin in the aortic arch were filled by a single injection. The left internal carotid artery in 127 out of 128 patients having bilateral subclavian catheterization was visualized by direct puncture of the left common carotid artery.

When all four main vessels were to be visualized, the arteriographic procedure was carried out in one session. General anesthesia was employed in 120 patients, particularly those in whom it was difficult to obtain cooperation and especially when serial bilateral carotid arteriograms were desired. In 72 patients in whom the procedure was performed under local anesthesia, the premedication consisted of demerol 25 mg., atropine 0.4 mg., and nembutal 50 to 100 mg., administered 30 minutes beforehand.

The number of injections, the number of patients, and the minimum and maximum amounts of conray 60 per cent injected in each arteriographic procedure are summarized in Table III. In the 192 patients studied, 1,133 injections were carried out and a total of 21,732 ml. of conray 60 per cent was injected.

RESULTS AND DISCUSSION

Conray 60 per cent proved to be a very satisfactory contrast material for visualization of both extra- and intracranial vascular lesions and many other intracranial abnormalities (Fig. 1–6). In almost 100 per cent of cases the arterial visualization was good to excellent. In a few of them, however, visualization was not completely satisfactory on all roentgenograms, but this was due to technical defect rather than inadequacy of the contrast material.

Table III

No. of Injections	No. of Patients	Amount of Contrast Material per Case (ml.)	
		Minimum	Maximum
1	6	10	30
2	6	16	40
3	4	17	85
4	23	40	110
5	28	50	135
6	37	62	150
7	49	70	165
8	25	97	180
9	7	97	195
10	4	125	180
11	1	—	130
13	2	230	240

Table IV

No. of Cases	Side Effects
34	Warmth
23	Burning sensation and pain (moderate)
4	Headache (moderate)
2	Cutaneous manifestation
5	Taste
2	Lights in front of eyes

Among the 72 patients in whom the procedure was performed under local anesthesia, the side effects were minimal and transient (Table IV).

The burning sensation and pain are experienced in the anterior chest and upper extremity during subclavian injection and in the neck and face during common carotid injection, especially when the internal carotid is stenotic or occluded and most of the contrast material enters the external carotid artery. Some patients complained of pain in the shoulder or in the retrosternal area, which may have been due to irritation of the structures supplied by the transverse scapular and internal mammary arteries. The pain in the arm occurs mostly in the elbow and hand. It is not severe and lasts no more than 5 to 15 seconds.

Occipital headache occurred during this procedure in 4 patients who had complete occlusion or marked stenosis of the internal carotid artery and in whom the occipital artery had undergone compensatory enlargement. This type of headache persisted no longer than 5 to 8 minutes. In patients in whom intramural injection or extravasation of contrast material occurred, pain near the site of injection did not last more than 1 to 3 minutes. It is interesting that when using conray, the patient experiences pain 6 to 10 seconds after the injection,

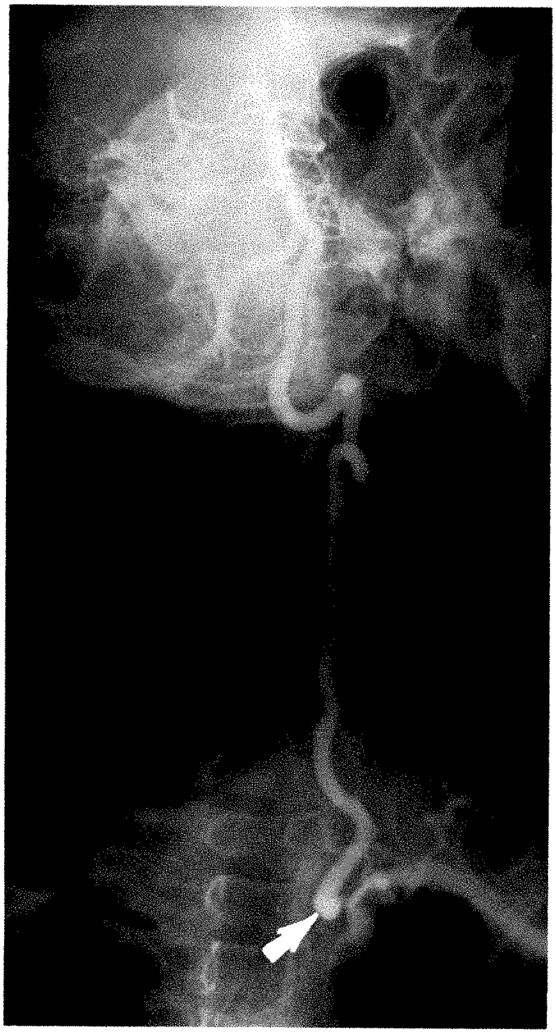


Fig. 1. Infraclavicular catheterization of left subclavian artery showing marked stenosis of left vertebral and subclavian arteries, normal appearance of basilar artery and its branches, and retrograde filling of distal segment of right vertebral artery.

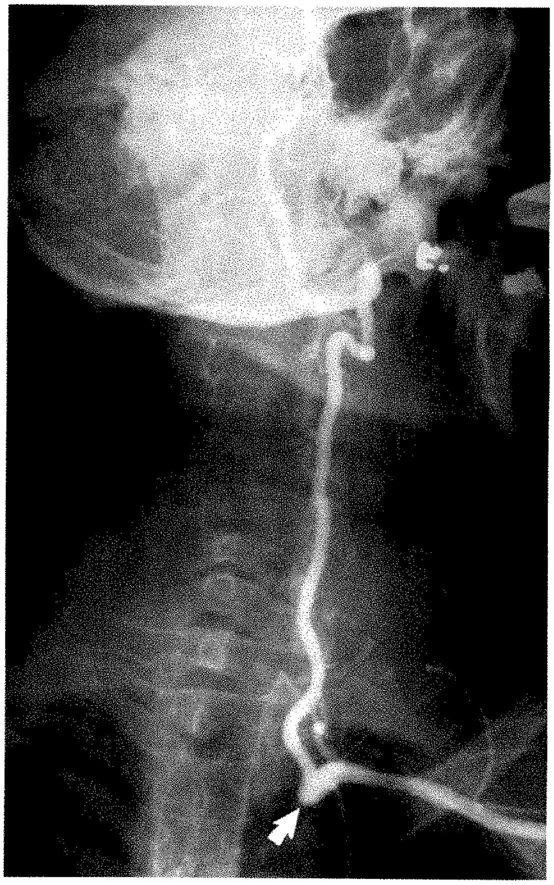


Fig. 2. Complete occlusion of left subclavian artery just proximal to origin of vertebral artery demonstrated by infraclavicular catheterization of subclavian artery.

which makes it possible to obtain satisfactory exposure even when serial arteriograms are made under local anesthesia. The pain produced by injection of sodium diatrizoate 50 per cent appears earlier, is more intense, and lasts longer, particularly when intramural injection or extravasation occurs. When intramural injection or extravasation of conray occurred, its reabsorption lasted 25 to 45 minutes, which is 10 to 20 minutes longer than that which occurs when using sodium diatrizoate.

Flushing was not observed, but slight conjunctival vasodilatation was regularly noted in all patients in whom direct injection of the common carotid was performed. One patient of whom the arteriograms were made under general anesthesia developed a generalized urticarial eruption 4 hours after the procedure. In another case, punctiform petechial hemorrhages in the skin over the right shoulder and upper extremity appeared several hours after injection of the right subclavian artery under local anesthesia.

In some patients, injection of 30 ml. of conray 60 per cent in the proximal segments of the innominate and left subclavian arteries and in the aorta was followed by a sensation of warmth radiating over the area supplied by these two vessels and, when the contrast material was injected directly

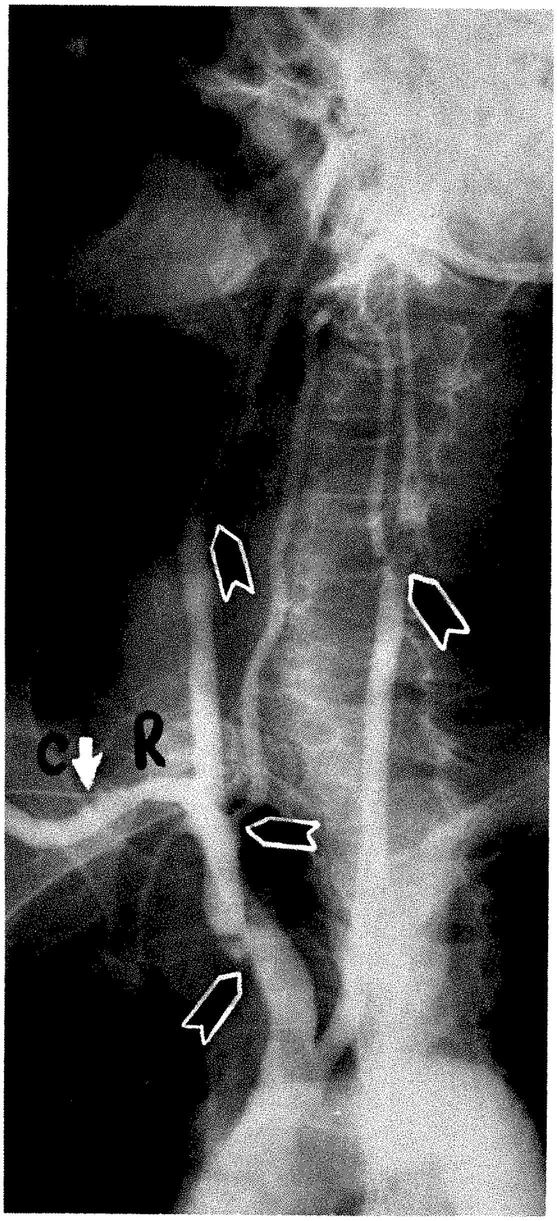


Fig. 3. Infraclavicular catheterization of right subclavian artery. Injection of 30 ml. of contrast material at level of origin of innominate artery showing stenosis of left and right internal carotid arteries at level of bifurcation of common carotids and stenosis of origin of right vertebral and right subclavian arteries.

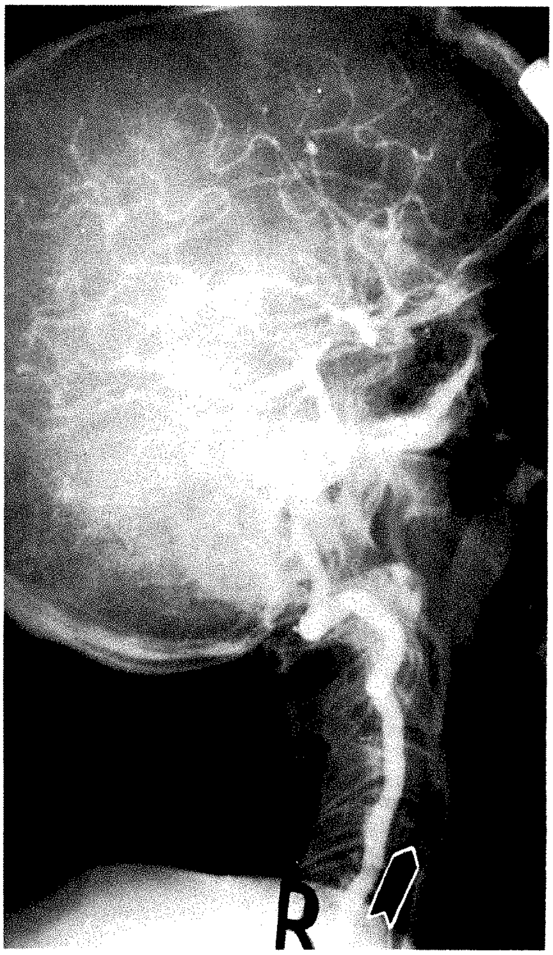


Fig. 4. Right subclavian arteriogram showing filling of right vertebral and collateral circulation through circle of Willis. Arrow points to complete occlusion of right internal carotid artery.

→

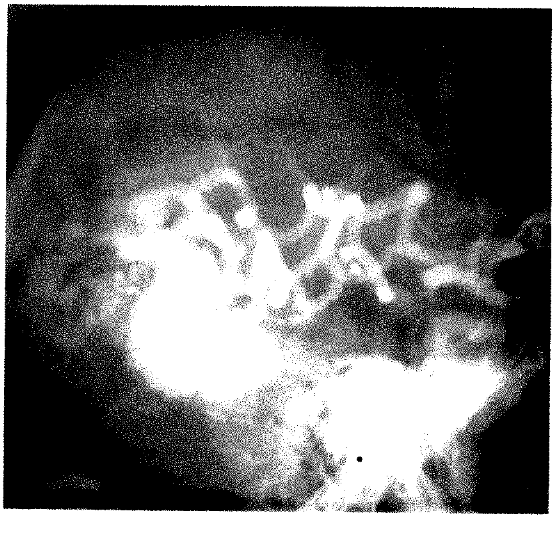


Fig. 5. Arteriovenous malformation of right hemisphere is demonstrated by injection of right carotid artery.

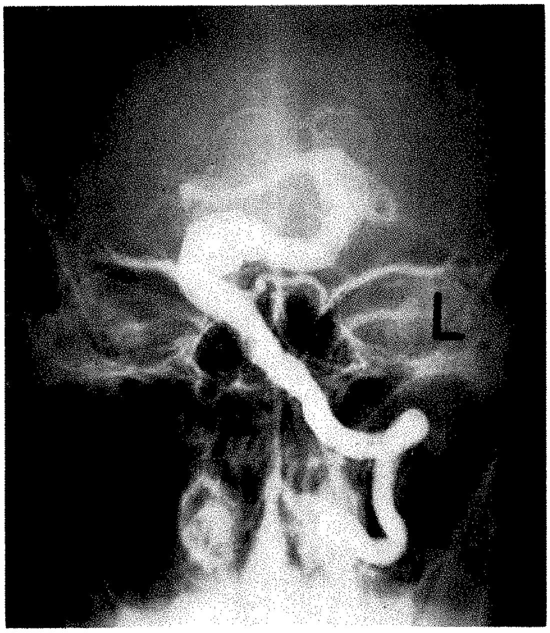


Fig. 6. Tortuous fusiform aneurysm of left vertebral and basilar arteries is demonstrated by infraclavicular catheterization of left subclavian artery.

into the aorta, over both lower extremities.

In 6 patients the tip of the catheter was inadvertently placed in the lumen of the vertebral artery, and the patients received an injection in this artery ranging from 10 to 20 ml. without any side effects other than "bright lights in front of the eyes" in 2 patients. In another patient in whom the subclavian and innominate arteries were tortuous, the tip of the catheter entered the common carotid artery rather than the proximal segment of the innominate artery, and 30 ml. of contrast material was injected. This was associated only with a sensation of warmth over the right side of the face. We have had no cerebral or local complications, either secondary to injection of conray or following its intramural injection or extravasation.

SUMMARY

1. Conray 60 per cent has been used for cerebral angiography in 192 patients and appears to be a satisfactory, well tolerated contrast material for this purpose.

2. Technically, there was little difference between the contrast obtained with sodium diatrizoate 50 per cent and conray 60 per cent; however, conray 60 per cent was better tolerated by patients under local anesthesia.

3. Side effects of conray 60 per cent were minimal and transitory even when large amounts were injected during a panarteriographic procedure carried out in one session.

William S. Fields, M.D.
Baylor University College of Medicine
Texas Medical Center
Houston, Texas

REFERENCES

1. Beall, A. C., Jr., Henly, W. S., Morris, G. C., Jr., Crawford, E. S., Cooley, D. A., and DeBakey, M. E. Translumbar aortography; simple, safe technic. To be published.
2. Bernstein, E. F., Reller, C. R., and Grage, T. B. Experimental studies of angio-conray; new angiographic agent. *Radiology*, 1962, *79*, 389–394.
3. Dotter, C. T., Straube, K. R., Bilbao, M. K., and Hinck, V. C. New contrast medium for intravascular use. *Northwest Med.*, 1962, *61*, 41–46.
4. Henly, W. S., Morris, G. C., Jr., Balas, P. E., and DeBakey, M. E. Vertebral arteriography by an infraclavicular route. To be published.
5. Hinck, V. C., and Dotter, C. T. Cerebral angiography with 60 percent conray; preliminary report. *J. Neurosurg.*, 1962, *19*, 312–313.
6. Marshall, T. R., and Ling, J. T. Clinical evaluation of two new contrast media; conray and angio-conray. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1963, *89*, 423–431.
7. Shealy, C. N. Comparison of renografin and hypaque for carotid arteriography. *J. Neurosurg.*, 1963, *20*, 137–138.
8. Smolik, E. A., and Nash, F. P. Cerebral angiography with new contrast medium (conray). *Missouri Med.*, 1962, *59*, 863–866.
9. Steinberg, I., and Evans, J. A. Conray; new cardiovascular and urographic contrast medium. *Radiology*, 1962, *79*, 395–400.
10. Weibel, J., and Fields, W. S. Direct percutaneous infraclavicular catheterization of subclavian artery. *J. Neurosurg.*, 1963, *20*, 233–237.
11. Weibel, J., and Fields, W. S. Technic of direct percutaneous infraclavicular catheterization of subclavian artery; report of 100 cases. To be published.

SODIUM IOTHALAMATE, ANGIO-CONRAY, IN SELECTIVE ANGIOGRAPHY*

FURTHER EVIDENCE OF LOW TOXICITY

By J. GERARD MUDD, M.D., *and* VALLEE L. WILLMAN, M.D.
ST. LOUIS, MISSOURI

SODIUM iothalamate,* a radiopaque contrast agent used in angiography has a low viscosity, (8.4 centipoise at 37.5° C.) and a high iodine content (48 per cent). These characteristics recommend it as a promising contrast agent. A few reports to toxicity and adverse reactions of varying severity have brought this agent under suspicion. Our favorable experience in 329 patients receiving 711 injections of sodium iothalamate (angio-conray) into the vascular system prompts this report.

METHOD OF STUDY

In the 329 patients under consideration, selective angiography was performed by way of right heart catheterization or percutaneous retrograde arteriography. The majority of these patients were under 10 years of age (Table I). The dosage was 0.5 to 1.0 ml. per kg. with a maximal dose of 35 cc. Larger amounts of the contrast agent were not necessary because of the proximity of the catheter to the lesion being studied. Hand injection was satisfactory for small amounts. Power injection was used for large volumes. In all instances the injection time was under 2 seconds. The patients were unanesthetized; sedated with morphine sulfate, sodium phenobarbital and hydroxyzine hydrochloride.†

Each patient was informed of the impending warm sensation and the possibility of coughing.

Multiple injections were made in 190 patients. As many as 6 injections were made (Table II) in some. The sites of injection are listed in Table III.

Table I

AGE OF PATIENTS RECEIVING INJECTION OF SODIUM IOTHALAMATE

Right Heart Catheterization	No. of Patients
1 da.–1 mo.	18
1–6 mo.	41
6–12 mo.	22
1–5 yr.	78
5–10 yr.	39
10–20 yr.	48
20–40 yr.	15
40 and over	10
Percutaneous Retrograde Arteriography	
1–5 yr.	1
5–10 yr.	2
10–20 yr.	6
20–40 yr.	17
40 and over	32
Total	329

RESULTS

There was no evidence of untoward reactions in spite of the proximity of the contrast medium to the heart and cerebral vessels. The usual flushing and transient tachycardia followed each injection. The only electrocardiographic abnormality observed was a transient T wave inversion in 1 patient with aortic stenosis in whom 20 ml. was injected just above the aortic valve. Transient increase in heart rate occurred in all cases and returned to the original rate in 1 minute.

---

* Angio-Conray supplied by Mallinckrodt Chemical Works.
† Vistaril.

* From the Cardiac Catheterization Laboratory of the Center of Cardiovascular Research, St. Louis University Medical Center, St. Louis, Missouri.

TABLE II

INJECTIONS PER PATIENT

No. of Injections	No. of Patients
1	139
2	73
3	70
4	27
5	12
6	8

Note: 711 injections in 329 patients.

Coughing occasionally resulted when the injection was into the pulmonary artery. This was of short duration and uncomplicated. It is not quite clear whether the coughing is a direct result of the sodium iothalamate or the rapid injection. This is currently being investigated.

Repeated injections were well tolerated. None of the patients experienced nausea or vomited. Adequate sedation with the addition of hydroxyzine hydrochloride is perhaps helpful in eliminating these complications.

In a number of infants with cardiac failure and pulmonary congestion, the use of sodium iothalamate did not measurably compromise cardiorespiratory function.

DISCUSSION

Sodium iothalamate, a new roentgenographic contrast agent has been received by the radiologist and cardiologist with varied acceptance. Initial reports of its use experimentally by Dotter *et al.*,[3] Foster *et al.*,[4,5] and Sessions *et al.*[8] indicated that this agent was less toxic than any currently available concentrated angiographic contrast media. Dotter *et al.* reported the use of sodium iothalamate 80 per cent in 270 patients for cardiovascular visualization and the lesser concentration meglumine iothalamate 60 per cent in 152 patients for cerebral angiography. He concluded that if further clinical experience confirms its relative safety and freedom from side effects, sodium iothalamate might become the "drug of choice." Renal and spinal cord tolerance to the medium was found to be satisfactory experimentally by Bernstein and his colleagues.[1] Further studies in the experimental animal by Bernstein *et al.*[2] also indicated its low toxicity. In a clinical trial of 44 patients, however, 11 per cent had cardiac complications; these consisted of ventricular fibrillation in 4 with recovery and death in 1 infant with multiple cardiac malformations. Further clinical trials by Steinberg and Evans[10] using mainly venous injection for renal and cardiovascular study, resulted in 6 severe reactions in approximately 400 patients (1.5 per cent). Smolik and Nash[9] reported less cerebral damage from meglumine iothalamate 60 per cent than from diatrizoate sodium 50 per cent. Kanick and Finby[6] obtained good results without toxic reactions in 100 consecutive cases. Marshall and Ling[7] reported on a large series of over 1,000 examinations using conray and angioconray with good opacification without serious toxic side effects.

In this study 329 patients received 711 injections of sodium iothalamate with no severe complication. These selective injections were made mainly into the heart. Injections into the aorta for renal or coronary artery studies did not result in any measurable abnormality in renal or cardiac function. Occasional coughing with rapid injection into the pulmonary artery was annoying but did not result in any respira-

TABLE III

SITE OF INJECTIONS OF SODIUM IOTHALAMATE

Leg vein	9
Arm vein	15
Veins within 10 cm. of right atrium	15
Right atrium	30
Right ventricle	213
Pulmonary artery	141
Left atrium	112
Left ventricle	31
Aorta	145
Total	711

tory distress or pulmonary complications. Electrocardiographic changes were not unusual for selective cineangiography.

No instance of fibrillation, hypotension, or cardiac arrest, as described by Bernstein *et al.*[2] and Steinberg and Evans[10] were encountered in our clinical studies.

Sodium iothalamate produced adequate contrast on the roentgenogram. The lower viscosity made it quite easy to inject by hand for the smaller patients. The viscosity was further reduced by bringing the temperature of the medium to approximately 38° C. before injection.

SUMMARY

Sodium iothalamate, angio-conray, was studied in 329 patients with a total of 711 injections. The contrast medium was injected into the heart by right heart catheterization, or into the aorta by percutaneous retrograde aortography. Multiple injections were made in the majority of cases.

There was no serious side reaction in any case. The usual flushing, transient tachycardia and occasional coughing were elicited. No hypotension, cardiac arrest or fibrillation was encountered.

This study indicates that angio-conray in our hands has been safe for multiple injection within the heart chambers or aorta.

J. Gerard Mudd, M.D.
St. Louis University School of Medicine
1325 South Grand Boulevard
St. Louis 4, Missouri

REFERENCES

1. Bernstein, E. F., Mackey, G. C., Emmings, F. G., and Amplatz, K. Experimental evaluation of renal and spinal cord tolerance to new angiographic agent, angio-conray. *Surgery*, 1962, *51*, 663–667.
2. Bernstein, E. F., Reller, C. R., and Grage, T. B. Experimental studies of angio-conray; new angiographic agent. *Radiology*, 1962, *79*, 389–394.
3. Dotter, C. T., Straube, K. R., Bilbao, M. K., and Hinck, V. C. New contrast medium for intravascular use. *Northwest Med.*, 1962, *61*, 41–46.
4. Foster, J. H., Winfrey, E. W., III, Sessions, R. T., and Killen, D. A. Clinical and experimental evaluation of angiographic contrast media. Presented at the Annual Meeting of the American Medical Association, Chicago, Ill., June 25–29, 1962.
5. Foster, J. H., Winfrey, E. W., III, Killen, D. A., and Sessions, R. T. New angiographic contrast medium, sodium iothalamate 80 percent: clinical and experimental evaluation. *J.A.M.A.*, 1962, *182*, 1009–1013.
6. Kanick, V., and Finby, N. Angio-conray; new angiographic contrast agent. *Radiology*, 1963, *80*, 438–443.
7. Marshall, T. R., and Ling, J. T. Clinical evaluation of two new contrast media; conray and angio-conray. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1963, *89*, 423–431.
8. Sessions, R. T., Winfrey, E. W., Killen, D. A., and Foster, J. H. Experimental evaluation of new angiographic contrast medium. *Surg., Gynec. & Obst.*, 1962, *115*, 187–190.
9. Smolik, E. A., and Nash, F. P. Cerebral angiography with new contrast medium (conray). *Missouri Med.*, 1962, *50*, 863–866.
10. Steinberg, I., and Evans, J. A. Conray: new cardiovascular and urographic contrast medium. *Radiology*, 1962, *79*, 395–400.

AN X-RAY TELEVISION IMAGE STORAGE APPARATUS*

By GEORGE BERCI, M.D., *and* ALBERT J. SEYLER, M.E.E., S.M.I.R.E.(Aust.)†
MELBOURNE, AUSTRALIA

TELEVISION as a means of displaying an x-ray image is by now well known and is widely used for this purpose in diagnostic radiology. Experience has shown that it has, in many applications, obvious advantages over conventional fluoroscopy.

The impetus to exploit television to this end came mainly from the introduction of electronic image intensification; for television made it possible to circumvent some of the obvious disadvantages of the image intensifier technique. However, it is true that the image quality presently obtainable is inferior to that which is available using standard roentgenographic techniques. Nevertheless, in many applications this loss of image quality is acceptable when, in exchange, the picture is immediately available for viewing under normal ambient lighting conditions. There is the further advantage that the image can be seen by several observers at the same time and that it can be recorded photographically.

It is common to all fluoroscopic techniques of x-ray image presentation, whether with or without image intensification and television, that the object is exposed to radiation for as long as the image is to be displayed. In many cases, particularly when no or only slow movement is being followed, the presentation time is primarily governed by the time required by the observer to examine the details of the image. Consequently, it seemed possible that we might be able to reduce the radiation dosage if we could achieve a temporary image retention, that is, "storage," without obviating the advantages of the x-ray television method. Thus the x-ray exposure time would be determined only by the time required for writing the image into the storage apparatus. It could then be viewed without any further radiation being applied for as long as the stored image would persist or be required. Of course, the time-proportional reduction in dosage would only be achieved if, during the exposure, the x-ray density was the same as for television display without storage. This would be the case if the storage device employed was able to accept the same electrical television signals as any normal television display device.

To explore the medical potential of this idea which has also been suggested by others,[3,7,8] we had a storage apparatus constructed in the Department of Surgery of the University of Melbourne.

THE STORAGE SYSTEM

Since the design of our storage system has been described in another paper,[9] only a brief reference will be made here to its basic features. For our experiments an industrial television Vidicon camera optically coupled to the output screen of a 5″ image intensifier (Philips) by means of a tandem-optic (Schneider) serves as an x-ray television signal source (Fig. 1). (It may be pointed out that any other x-ray television equipment supplying standard television signals will serve for this purpose.) The camera is controlled in the usual way from a Central Camera Control Unit (Fernseh) which in our case has the added facility of allowing one to switch, in turn, from one to another of five different cameras (Fig. 2). This is particularly convenient if different aspects of the object are to be displayed alternately. It is possible by using two image intensifiers and two television cameras to record a roentgenogram made in an anteroposterior plane and in the lateral plane consecutively.

---

* From the Department of Surgery, University of Melbourne, Royal Melbourne Hospital, Melbourne, Australia.

Based on a paper presented at the Tenth International Congress of Radiology, August 25–September 1, 1962, Montreal, Quebec, Canada.

† Research Laboratories, Postmaster-General's Department, Australia.

A Synchronizing Pulse Generator of the type used in 625-line standard television equipment controls not only the camera chain, but all other timing functions inherent in the operation of the x-ray and storage apparatus. These timing functions are derived in a special Timing and Control Unit and are governed primarily by the characteristics of the storage device which we are using in our apparatus and which forms the heart of the Storage Unit (Fig. 3). After careful review of the other possible alternatives, we have chosen for this purpose an electronic storage tube[6] (type Raytheon QK 685). Our primary reason for its selection was that it was readily available in commercial production; moreover, by its use there seemed to be no risk of significant loss in image quality. It would also make it possible for us to display the stored image on any number of standard television monitors and to retain it for periods of up to half an hour.

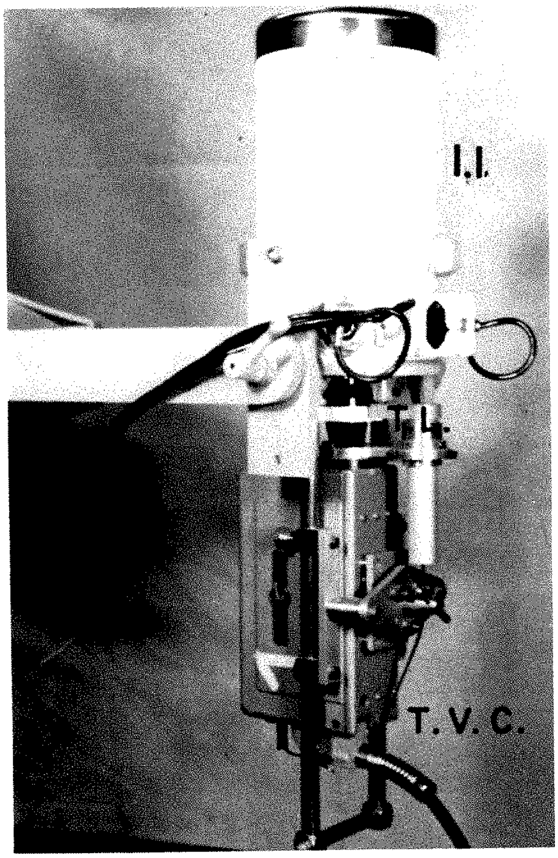


Fig. 1. Image Intensifier (I.I.) coupled to the Vidicon Camera (T.V.C.). The Tandem Lens (T.L.) is focused by remote control.

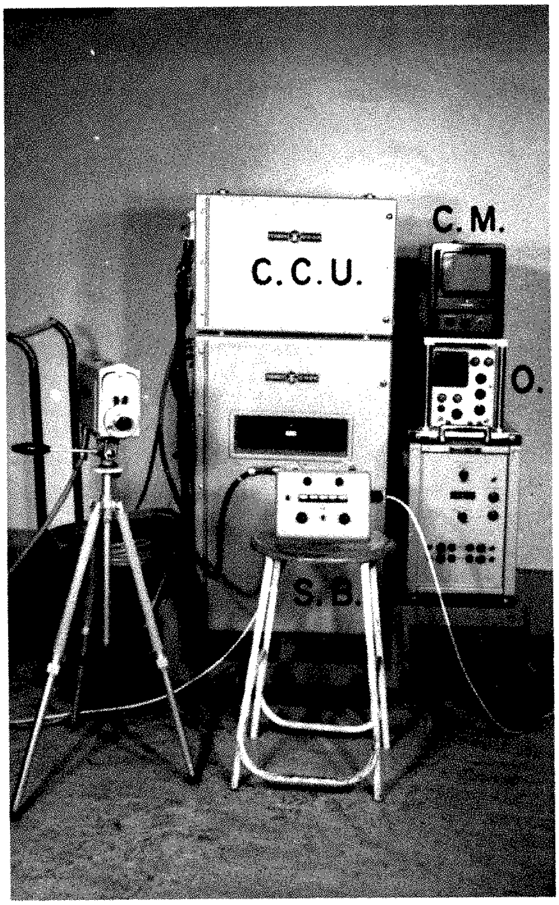


Fig. 2. Central Camera Control Unit (C.C.U.) which controls up to 5 different cameras consecutively. In front the push button Switching Box (S.B.) is visible. The Control Monitor (C.M.) for the operator with Oscilloscope (O) is at the right.

A rough experimental apparatus to test the feasibility of our ideas was completed and successfully demonstrated in August, 1960. The choice of this kind of storage tube determined the operation of the whole storage unit, because in order to store a new television image, the previously stored one must be erased, and the tube primed ready for acceptance of the new one, which is then written-in and thereafter is read and displayed. Thus, four distinct operations, erase, prime, write and read, are involved. All these intervals are made multiples of the television frame interval which is 40 milliseconds for our T.V. system. The total time for image changeover is equal to 12 frames, that is 0.48 second, and 3 frames of this are used for writing. Since an image signal is required only during the writing interval, we have timed the x-ray unit from the timing and control unit by switching the Bucky circuit remotely. With this method of x-ray timing, the actual "turning-on time" has to be advanced 2 to 3 frames (80 to 120 msec.) ahead of the writing interval to make certain that the re-

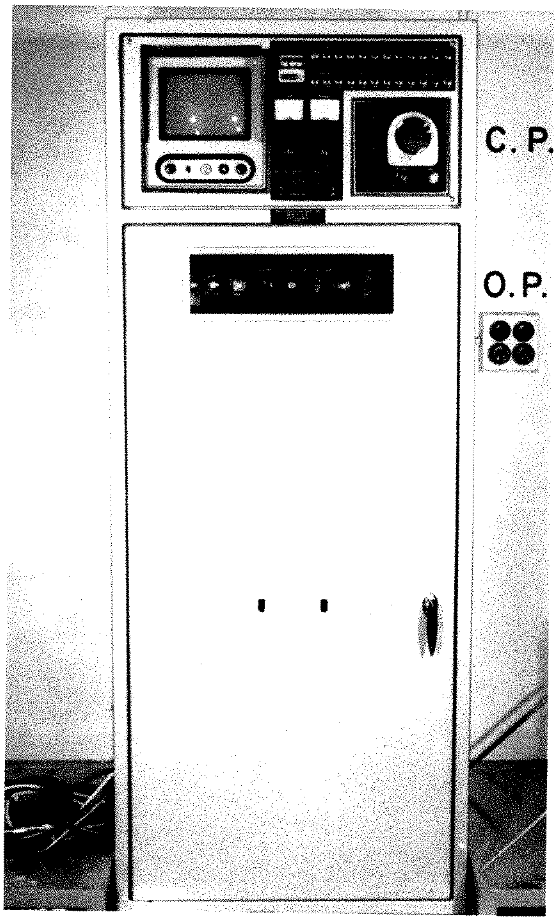


Fig. 3. Storage Unit, Control Panel (C.P.) with a monitor screen, oscilloscope and Operating Panel (O.P.).

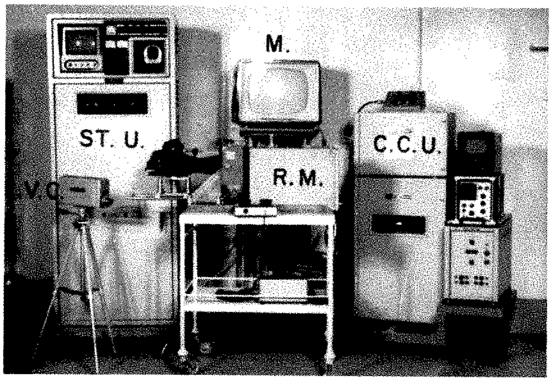


Fig. 4. Complete setup: Storage Unit (ST.U.), Television (Vidicon) Camera (T.V.C.), 17 inch Monitor (M.), Central Camera Control Unit (C.C.U.) with switching box on top, 16 mm. Arriflex camera mounted in front of Recording Monitor (R.M.).

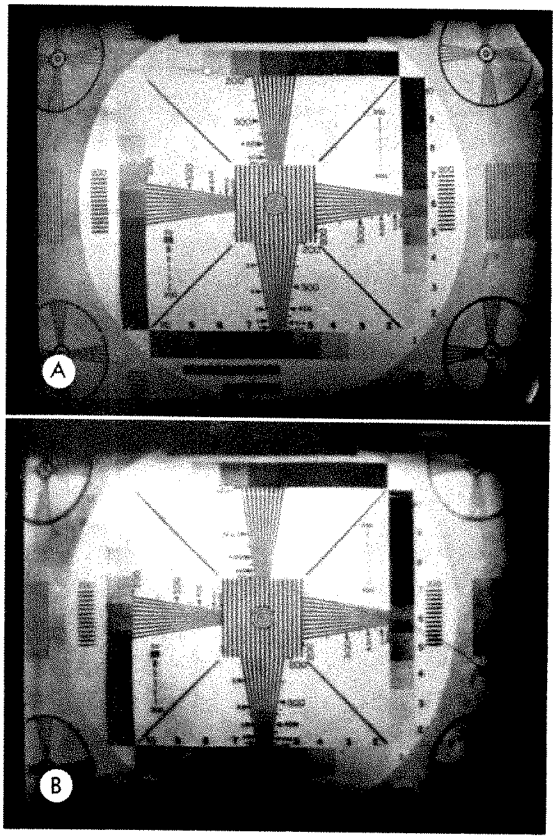


Fig. 5. (*A*) Retma Television Test Chart "*direct*" televised and as recorded from the television screen. (*B*) The same pattern as in *A*, but "*stored.*" A negligible loss in resolution is encountered in the storing process.

quired radiation output will be available during the writing interval. In the data which we are reporting later, we will always record the actual x-ray unit "on-time" and this may quote a somewhat higher energy than was actually applied.

All system functions are centrally controlled, if necessary from a different room, and only a single push button switch operation is required to effect an image storage when desired.

TEST RESULTS WITHOUT X-RAY

To enable us to test the apparatus without the image intensifier and x-ray source, we took the television camera (Vidicon) and placed it opposite a test pattern. Photographs were taken from a television receiver (EV 25) with a 10″ screen using a 35 mm. still camera. In Figure 5 *A* a Television Test Chart (Retma) is shown as televised directly and recorded from the screen. The same pattern under the same conditions but this time stored is shown in Figure 5 *B*. A negligible loss in resolution has been incurred in the storing process. Similarly, in Figure 6 *A* a photographic gray scale pattern has been directly televised and recorded. In contrast, in Figure 6 *B* the same pattern has been stored. It will be seen that there has been a compression of the gray scale in the darker shades.

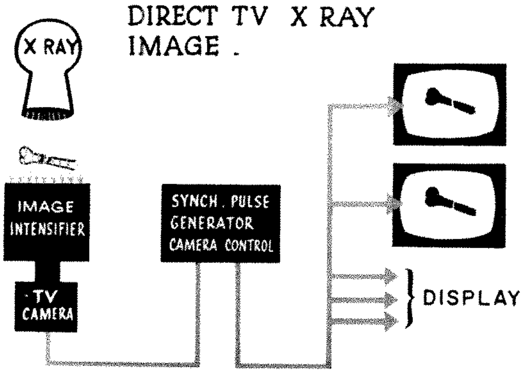


Fig. 7. Schematic diagram of a "*direct*" televised x-ray image.

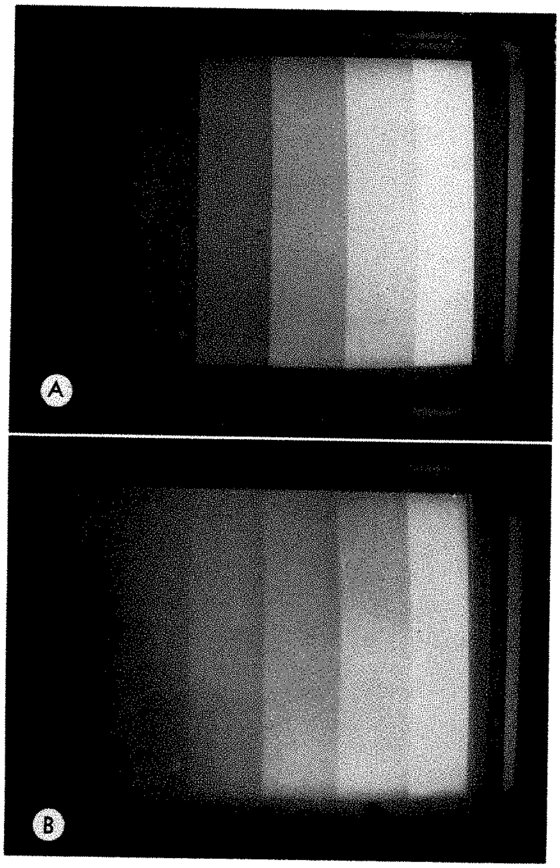


Fig. 6. (*A*) Photographic gray scale "*direct*" televised. (*B*) The same photographic gray scale pattern "*stored*." A gray scale compression in the darker shades is noticeable.

TEST RESULTS WITH X-RAY

In this test series an "Elema Pluromobile" x-ray unit was used, with "fine focus" adjustment and constant diaphragm open-

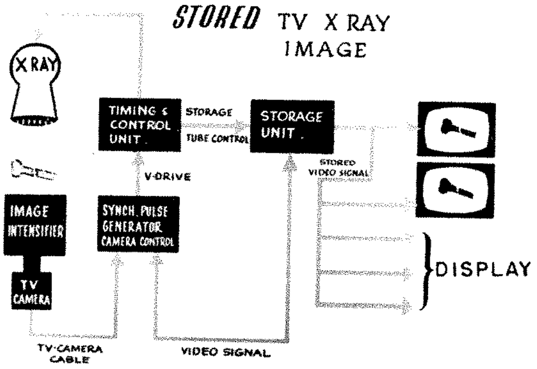


Fig. 8. Schematic diagram of a "*stored*" televised x-ray image.

ing, tube-object distance of 83 cm., 5″ image intensifier coupled to an industrial camera (Vidicon), Central Camera Control Unit and Storage Unit. The recording facilities were the same as those mentioned above.

"Direct" in this context means that the object is televised during continuous radiation as would be the case for normal television fluoroscopy (Fig. 7).

"Stored" image is that obtained from the storage tube in the reading mode after a short automatic exposure and displayed on the same monitor as the direct one (Fig. 8).

The resolution pattern employed consisted of two 90 mm. square Perspex plates, 3.5 mm. thick, in which grooves were milled to accommodate a series of round copper wires. These wires were arranged in groups having thicknesses of 0.8, 0.6, 0.4 and 0.3 mm. respectively, whereby in each group the spacing between the individual wires was equal to their thickness.

In Figure 9 *A* is shown a roentgenogram taken under standard conditions of a resolution test pattern using 60 mas. at 40 kv. with no grid. The same test pattern directly televised and recorded from the monitor, using 1 ma. continuous radiation at 60 kv., is shown in Figure 9 *B*. The 0.8 and 0.6 mm. wires have been resolved but those of 0.4 and 0.3 mm. now cannot be distinguished. In Figure 9 *C* the same pattern has been stored. The 0.8 and 0.6 mm. wires have been resolved so that we can almost match the resolution achieved by direct television but in order to obtain this image we had to use only 0.16 mas. radiation exposure.

Exposing a roentgenographic film without a grid under the same conditions and

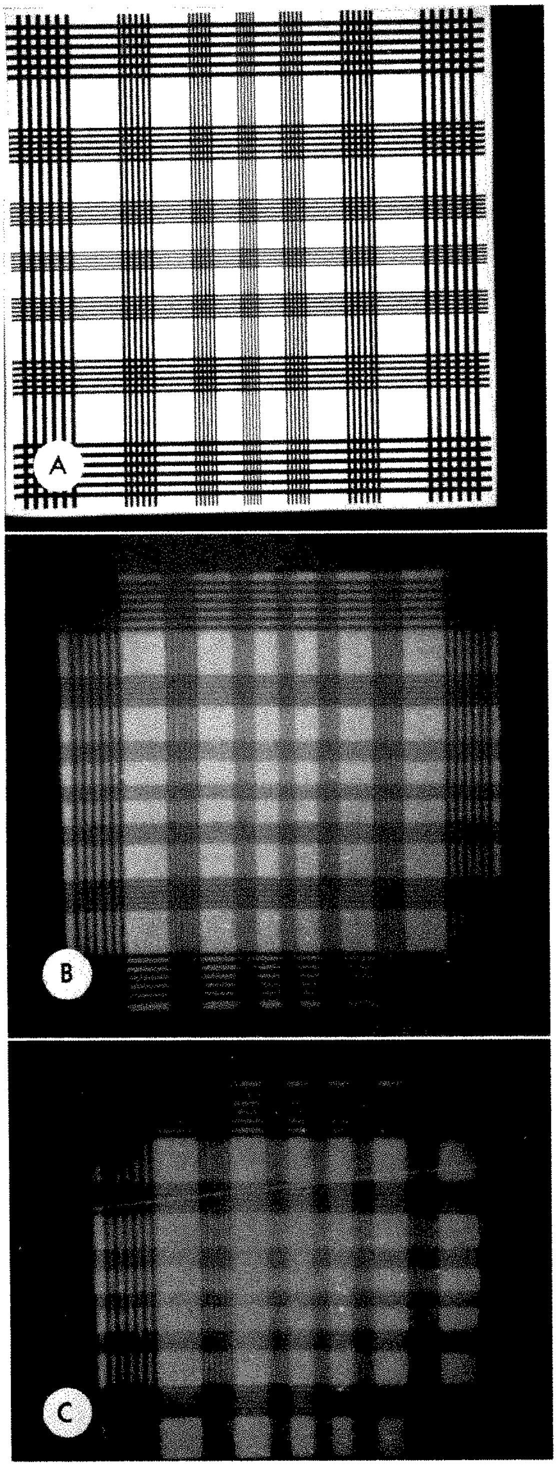


FIG. 9. (*A*) Roentgenogram of the resolution test pattern (60 mas., 40 kv., no grid). The wire thickness in each group is: 0.8, 0.6, 0.4, and 0.3 mm. (*B*) Resolution pattern "*direct*" televised. (1 ma. continuous radiation at 60 kv.). The wires of 0.4 and 0.3 mm. thickness cannot be resolved. (*C*) Resolution pattern "*stored*" (0.16 mas., 60 kv.); 0.8 and 0.6 mm. wires have been resolved.

using the same radiation exposure dosage as was used for the stored image gave us a roentgenogram that was so underexposed that it did not reveal the mesh pattern.

Figure 10 *A* is the roentgenogram of a density step pattern which was made in 7 steps in a 90×90 mm. square area consisting of 5 copper strips (0.8, 0.4, 0.2, 0.1 and 0.05 mm. thickness), the last step being left blank, and the first consisting of a lead strip. The film was exposed without a grid with a radiation current of 375 mas. at 40 kv. Figure 10 *B* shows the direct televised picture of the contrast pattern using 2 ma. continuous radiation at 90 kv. In Figure 10 *C* the picture of the same contrast pattern has been stored, using this time only 0.3 mas. at 90 kv. Again, there is evident a slight compression in the darker shades, that is, in the higher densities.

Where a roentgenographic film without a grid was exposed to the same radiation current as had been used for a stored image, no pattern was visible at all.

We have also tested two wax dummies or phantoms. The first contained as a central core part of the shaft of the femur. Above it we embedded two Kirschner wires, each 1.5 mm. thick, and below a Steinmann's pin, 3 mm. thick. In addition, a Kuntscher nail was partly introduced into the medullary cavity. To achieve a proper roentgenogram, 189 mas. at 60 kv. was employed, using a Smit grid (7:1 ratio).

Figure 11 *A* is a photograph of the femur dummy as directly televised and recorded from the screen using 2 ma. continuous radiation at 90 kv. For the stored image of the same object (Fig. 11 *B*), only 0.3 mas.

→

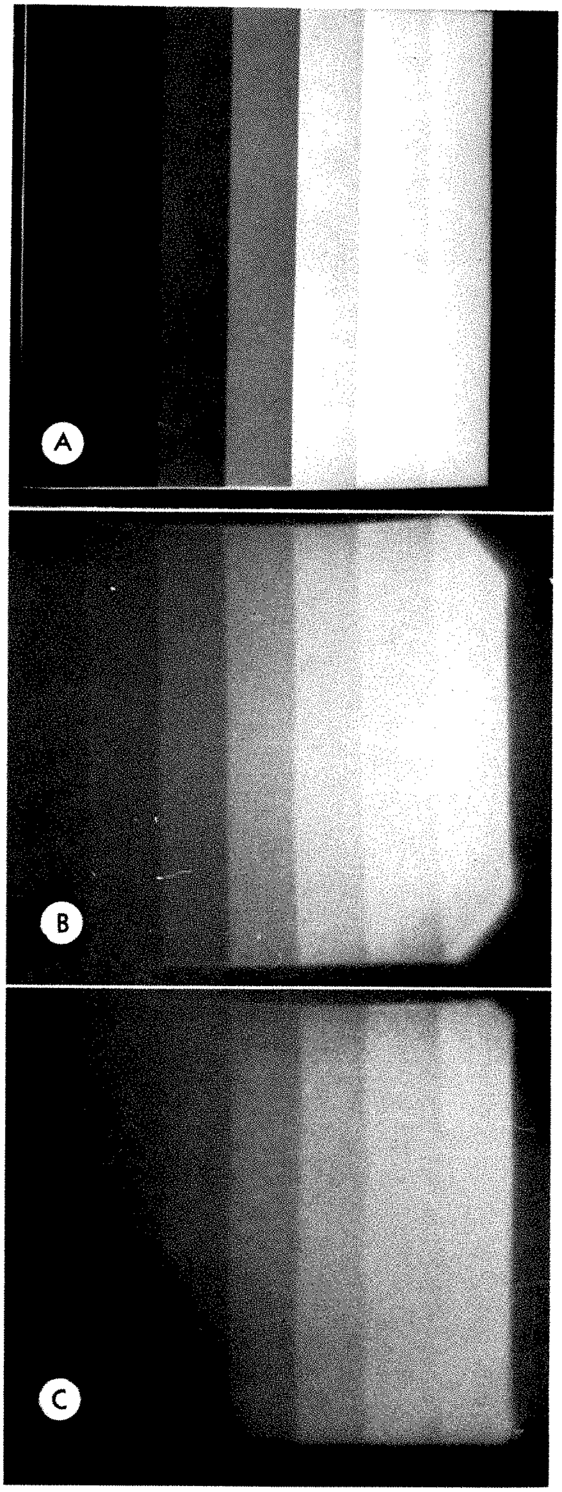


Fig. 10. (*A*) Roentgenogram of the density step pattern (375 mas. at 40 kv.), using 5 copper strips (0.8, 0.4, 0.2, 0.1 and 0.05 mm. thickness), the last step being left blank and the first consisting of a lead strip. (*B*) "*Direct*" televised density pattern (2 ma. continuous radiation at 90 kv.). (*C*) "*Stored*" density pattern (0.3 mas., 90 kv.). Slight compression in the darker shades.

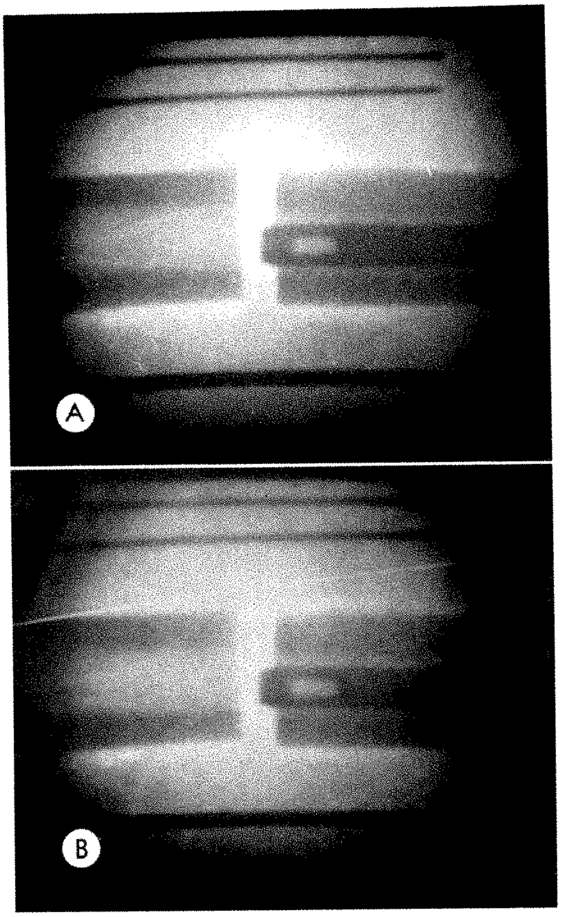


FIG. 11. (*A*) Femur wax dummy "*direct*" televised (2 ma. continuous radiation at 90 kv.), 2 Kirschner wires (each 1.5 mm. thick) above and a Steinmann's pin (3 mm.) below. (*B*) Femur wax dummy "*stored*" (0.3 mas., 90 kv.).

at 90 kv. was required. When a film was exposed without a grid and with the same radiation current as was required to achieve the stored image, the femur and pins were not recognizable.

The second wax phantom contained the head and neck of the femur. A wire, 1.3 mm. thick, was secured around the neck of the femur and some 1 mm. pins were placed beside it. To achieve a satisfactory roentgenogram 189 mas. at 68 kv. was required, using the same grid as before. For the direct television of this dummy we used 6 ma. continuous radiation at 95 kv. without a grid (Fig. 12 *A*). To enable us to obtain a stored x-ray image of the same object (Fig. 12 *B*), we required, without a grid, only 0.75 mas. at 95 kv. Again, with the exposure of the film without a grid and using the same phantom and the same roentgenographic data as mentioned above, no roentgenogram was obtained.

In Table 1, the test data which have been accumulated are shown.

AUTOMATIC CYCLING MECHANISM

By establishing a central unit for the control of all functions, it has been proved possible to effect image storage, as desired,

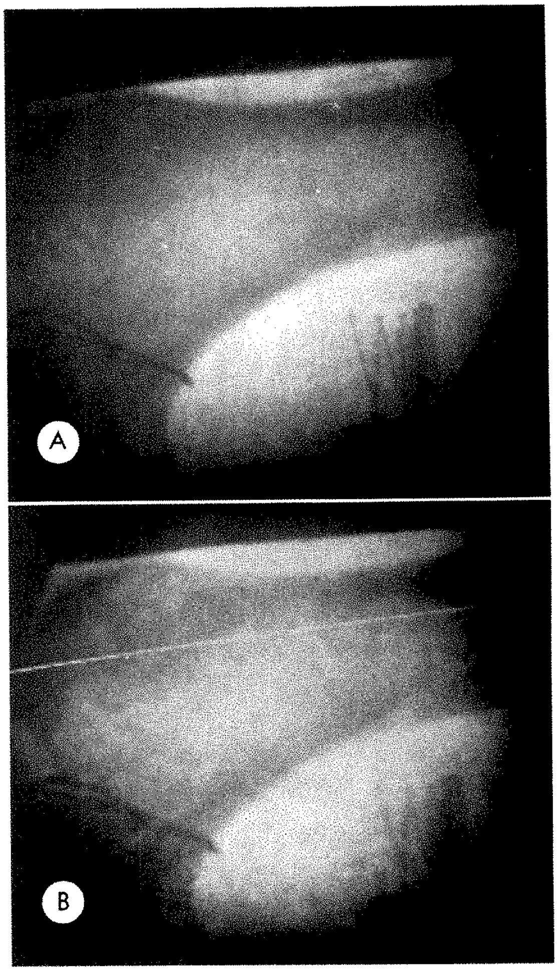


FIG. 12. (*A*) Wax dummy from a hip "*direct*" televised (6 ma. continuous radiation at 95 kv.). The wire around the neck of the femur is 1.3 mm. thick. A few tailor's pins (1 mm.) have been placed alongside for comparison. (*B*) The same wax dummy as in *A* "*stored*" (0.75 mas., 95 kv.).

Table I

Object	Mode of Presentation	X-Ray Data				
		kv.	ma.	Exposure Time (sec.)	mas.	Grid
Resolution pattern	Roentgenogram	40	60	1	60	No
	Direct televised	60	1	—	—	No
	Stored	60	1	0.16	0.16	No
Density step pattern	Roentgenogram	40	300	1.25	375	No
	Direct televised	90	2	—	—	No
	Stored	90	2	0.16	0.3	No
Wax femur dummy	Roentgenogram	60	300	0.63	189	Yes
	Direct televised	90	2.4	—	—	No
	Stored	90	2.4	0.12	0.3	No
Wax hip dummy	Roentgenogram	68	300	0.63	189	Yes
	Direct televised	95	6	—	—	No
	Stored	95	6	0.12	0.72	No

For all roentgenograms Kodak Bluebrand X-ray films were used with Auer-Universal intensifier screen, and where a grid was used, this was a Smit-grid 7:1 ratio.

by the operation of a single press button switch. This design has also facilitated the automatic sequencing of exposures ("cycling") at pre-set intervals varying between 1 and 6 seconds. The timing is schematically depicted in Figure 13.

Thus it is possible to observe slow moving events in pseudo-motion, a feature which should prove very useful in a number of applications as, for example, in making it easy to make serial observations during the manipulation of fractures, or during the insertion of an intramedullary nail or Smith-Petersen pin, where the progression of the nail can be followed at preselected intervals and corrected as necessary. Equally, it should be possible to follow step by step the introduction of radiopaque catheters. Furthermore, using two image intensifiers in biplane position, it is possible during cycling to change from an antero-posterior image to a lateral one merely by pressure of a button. This means that one stored image held, for instance, for 4 seconds displays the situation in one plane while the next picture demonstrates it in another.

We have made 16 mm. movie test film strips from the television screen, simulating the introduction of a Kuntscher nail into the femur dummy. A cycling interval of 6 seconds was adopted between consecutive pictures, each having 0.5 mas. exposure. (It was necessary to increase the radiation current by 0.2 mas. compared with that mentioned in Figure 11 *B* because a different x-ray machine was used.) A total of 12 pictures was stored in turn to allow for the complete visualization of the introduction

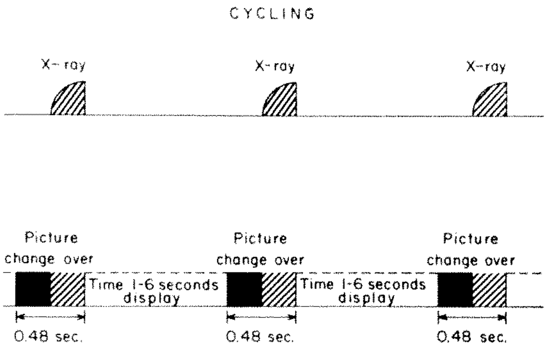


Fig. 13. Schematic diagram of the cycling periods. The intervals can be preselected (1–6 seconds).

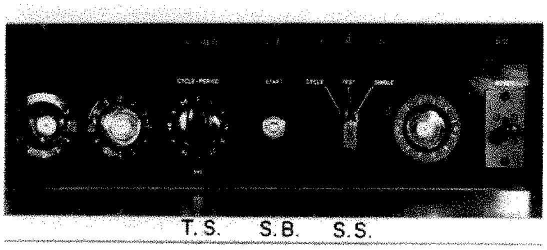


Fig. 14. Operating panel of the storage unit. Time Selector (T.S.) 1–6 seconds in 0.5 sec. intervals. Starter Button (S.B.) and Selector Switch (S.S.) for cycling, test or single picture positions.

of the Kuntscher nail. This necessitated a total over-all exposure of 6 mas. at 90 kv., as compared with 2,268 mas. for 12 roentgenograms for the same phantom, and using standard roentgenographic techniques.

DISCUSSION AND CONCLUSION

The introduction of the image intensifier technique opened a new era in diagnostic radiology by merit of the reduction in radiation which its use made possible. Moreover, the image was available for immediate viewing as well as for documentation on cinefilm. Some of the disadvantages of this technique were overcome by coupling television to the image intensifier but an important one still remained; namely, the limitation of the picture quality or resolution. There is, of course, a minimal loss of resolution each time an optical image is converted into an electronic one (or equally in the reverse direction). This loss is equally incurred when a television unit is introduced into the circuit. However, at present the image intensifier is still the main limiting factor of attainable resolution. It seemed, therefore, that we must limit the choice of applications in the medical field to those for which the performance of the equipment would prove satisfactory.

We freely admit that the x-ray television storage apparatus, which we are now reporting, is still in an experimental stage and that our clinical experience with it is very limited. The quality of the picture falls short of that which we hope ultimately to achieve. For example, we should be able to avoid compression in the gray scale by the introduction of a suitable "gamma" correction in the storage unit. The equipment, as it stands, is however, already capable of producing an image which will allow its immediate exploitation in certain fields, where the usefulness of the image intensifier is already accepted as, for example, in traumatology, orthopedic surgery and in facilitating combined methods of endoscopy.[2] Its use certainly makes it possible to achieve a substantial reduction in the radiation dosage and to inspect the image in different locations and in a form which makes it possible to record the image simultaneously. The cycling mechanism facilitates materially the roentgenologic control and observation of slow movements.

At this stage, when there is active development in television signal storage devices as well as in the technology of x-ray sources (pulsed or grid controlled units), in image intensification and in special x-ray television systems, we are uncertain in which direction the search for the ideal system will move, but from our experience thus far we have learned that any system which is to be developed will need to embrace certain basic features which we have been able to establish, using a fully automatic central control of all the components of the equipment.

We believe that a further development of this storage system will be the multiple image storage unit. This would mean that, for instance, four pictures could be stored using the same single storage tube, compared with each other as thrown, in turn, on a full size screen or visualized altogether on the 4 quarters of the full size screen (Fig. 15).

The need for further progress in the field of x-ray television storage equipment is quite obvious when one considers the advantages of its use in specific medical applications.[1]

A storage system will be successful only if it will fulfill the following prerequisites:

1. Substantial reduction of radiation.
2. Immediate image display on several monitors.
3. Persistent image storage, without significant loss of image quality.
4. Useful picture quality which is adequate for the purpose.
5. A storage cycling mechanism to make it possible to follow slow movements.
6. It must be tailored to the needs of hospital economy. The capital investment may be considerable but this could be compensated in the long run by a reduction in operating time. Since the running costs should be within the limits of a normal hospital budget, it should not require personnel with other than standard radiologic training for its operation.

SUMMARY

The results are presented of our early experience with an x-ray television storage apparatus. It is found that since the resolution capability of the storage tube (Raytheon QK 685) of this apparatus is superior to that of the image intensifier television system, there has been no noticeable loss of spatial resolution. Some compression of the gray scale has, however, been encountered in the stored image, although it should be possible to overcome this disturbance by suitable electronic correction. By utilizing a fully automatic central timing and switching control of all the system functions, it has proved possible to achieve a remarkable reduction in radiation exposure. A direct consequence of this is the practicability of presenting slowly moving events in stroboscopic sequence of 1 to 6 second exposure intervals without accumulating dangerous radiation dosage. The potential of this equipment has been outlined.

George Berci, M.D.
Department of Surgery
University of Melbourne
Royal Melbourne Hospital
Melbourne, Australia

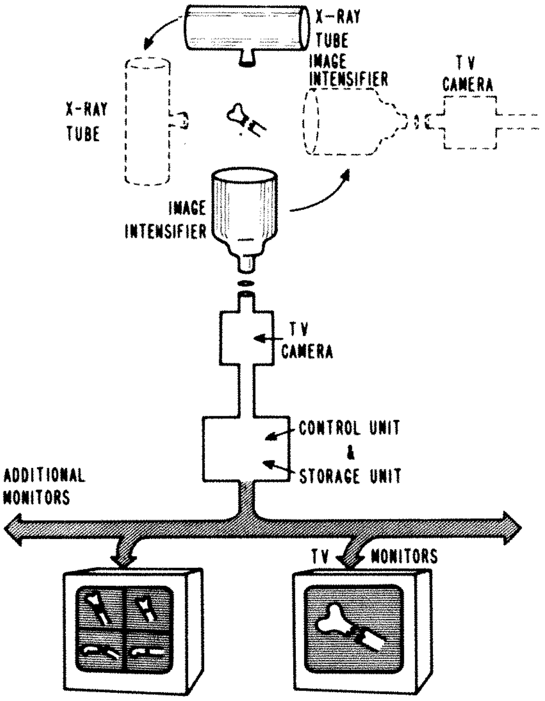


Fig. 15. Schematic diagram of a multiple (4) image storage unit, using the same single storage tube. Four pictures could be stored on the 4 quarters of the full size screen, or any one may be enlarged to the full screen size.

The authors wish to thank Professor M. R. Ewing of the Department of Surgery, University of Melbourne and Dr. H. A. Luke, Director of the Diagnostic X-ray Department of the Alfred Hospital for their help and encouragement. One of the authors (A.J.S.) is also indebted to the Director-General of the Postmaster General's Department for the permission to carry out this work. The construction and development of the present storage unit was undertaken by Mr. J. Davids and was supported by a grant from the Anti-Cancer Council of Victoria.

REFERENCES

1. Berci, G. Medicine and television. *M. J. Australia*, 1961, *48*, 1005–1010.
2. Berci, G., and Davids, J. Endoscopy and television. *Brit. M. J.*, 1962, *1*, 1610–1613.
3. Garthwaite, E., and Holey, D. G. X-ray image amplifier using image orthicon camera tube. *J. Brit. Inst. Radio Eng.*, 1959, *19*, 615–623.
4. Girdany, B. R., Gaither, E. S., and Darling,

D. B. Large screen image amplification with closed-circuit television employing television tape-recorder. *Radiology*, 1961, *77*, 286–291.

5. Heinz-Guenther, W. Aufzeichnung und Wiedergabe von Standbildern mit dem Folienspeicher. *Randfunktechn. Mitt.*, 1962, *6*, 106–110.
6. Hergenrother, R. C., Luftman, A. S., and Sawyer, C. F. Improved storage tube design. *Tele-tech. & Electronic Ind.*, 1956, *15*, 82–83.
7. Lubszinski, H. G. Survey of image storage tubes. *J. Sci. Instr.*, 1957, *34*, 81–88.
8. Schut, T. G., and Oosterkamp, W. J. Application of electronic memories in radiology. *Medicamundi*, 1959, *5*, 85–88.
9. Seyler, A. J. X-ray television system with image storage and automatic exposure release. *J. Brit. Inst. Radio Eng.*, 1962, *22*, 229–240.
10. Sturm, R. E., and Morgan, R. H. Screen intensification systems and their limitations. Am. J. Roentgenol. & Rad. Therapy, 1949, *62*, 617–634.
11. Wallman, H., and Wickbom, I. Roentgen-television equipment for use in surgery. *Acta radiol.*, 1959, *51*, 297–304.

Vol. 90, No. 6

THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

Editor: Traian Leucutia, M.D.
Assistant to the Editor: Kenneth L. Krabbenhoft, M.D.
Associate Editors: Harry Hauser, M.D., Russell H. Morgan, M.D., Edward B. D. Neuhauser, M.D., Wendell G. Scott, M.D.
Consulting Editorial Board: See front cover.
Published by: Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Illinois.

Issued monthly. Annual subscription: United States, Mexico, Cuba, Central and South America, and Canada $15.00; other countries, $17.00. Current single numbers, $1.50. Advertising rates submitted on application. Editorial office, 110 Professional Building, Detroit 1, Michigan. Office of publication, 301–327 East Lawrence Avenue, Springfield, Illinois. Information of interest to authors and readers will be found on page ii.

AMERICAN ROENTGEN RAY SOCIETY

President: R. M. Caulk, Washington, D. C.; *President-Elect:* H. O. Peterson, Minneapolis, Minn.; *1st Vice-President:* J. E. Miller, Dallas, Tex.; *2nd Vice-President:* D. L. McRae, Montreal, Que., Canada; *Secretary:* C. A. Good, Mayo Clinic, Rochester, Minn.; *Treasurer:* S. W. Brown, 1467 Harper Street, Augusta, Ga.

Executive Council: R. M. Caulk, H. O. Peterson, J. E. Miller, C. A. Good, S. W. Brown, C. B. Holman, J. S. Dunbar, J. F. Roach, H. G. Reineke, D. G. Mosser, J. C. Cook, E. E. Barth, T. Leucutia, S. F. Ochsner, J. D. Reeves, H. M. Stauffer, T. F. Leigh, J. P. Medelman, Chairman, 110 Birchwood Ave., Birchwood, White Bear Lake 10, Minn.

Program Committee: C. A. Good, J. F. Roach, T. Leucutia, J. S. Dunbar, J. P. Medelman, D. G. Mosser, H. O. Peterson, Chairman, Minneapolis, Minn.

Publication Committee: J. A. Campbell, M. M. Figley, R. N. Cooley, J. F. Holt, J. F. Roach, Chairman, Albany, N. Y.

Finance and Budget Committee: H. M. Stauffer, T. F. Leigh, J. R. Danstrom, R. E. Parks, C. B. Holman, Chairman, Rochester, Minn.

Committee on Scientific Exhibits: J. O. Reed, R. R. Greening, J. S. Dunbar, Chairman, Montreal, Que., Canada.

Advisory Committee on Education and Research: A. Raventos, A. R. Margulis, E. C. Lasser, F. J. Bonte, H. G. Reineke, Chairman, Cincinnati, Ohio.

Representatives on the American Board of Radiology: C. A. Stevenson, Spokane, Wash.; J. F. Roach, Albany, N. Y.; C. A. Good, Rochester, Minn.

Director of Instruction Courses: D. G. Mosser, Minneapolis, Minn.

Manager of the Annual Meeting: J. C. Cook, 110 Professional Building, Detroit, Mich. 84201

Editor: T. Leucutia, 110 Professional Building, Detroit, Mich. 84201

Sixty-fifth Annual Meeting: Radisson Hotel, Minneapolis, Minn., September 29 to October 2, 1964.

AMERICAN RADIUM SOCIETY

President: Charles G. Stetson, Tenafly, N. J.; *President-Elect:* Joseph H. Farrow, New York, N. Y.; *1st Vice-President:* Juan A. del Regato, Colorado Springs, Colo.; *2nd Vice-President:* John L. Pool, New York, N. Y.; *Secretary:* Justin J. Stein, Los Angeles, Calif.; *Treasurer:* Milton Friedman, 1016 Fifth Ave, New York 28, N. Y.

Executive Committee: Jesshill Love, Chairman; Robert L. Brown; Gilbert H. Fletcher; Charles G. Stetson; Justin J. Stein; Joseph H. Farrow; Juan A. del Regato; John L. Pool; Milton Friedman.

Scientific Program Committee: Charles G. Stetson, Chairman; A. N. Arneson, St. Louis, Mo.; Milton Friedman, New York, N. Y.; Harold E. Johns, Toronto, Ont.; Henry S. Kaplan, Palo Alto, Calif.; Calvin T. Klopp, Washington, D. C.; Milford D. Schulz, Boston, Mass.; Joseph H. Farrow, Ex officio.

Committee on Arrangements: Henri LeClaire, Chairman, Cincinnati, Ohio; Manuel Garcia, Chairman Designate, New Orleans, La.; Albert L. Allen, Huntington, W. Va.; Robert D. Berkebile, Elyria Ohio; H. Peter Mueller, Belmont, Mass.; Ralph M. Scott, Louisville, Ky.; Milton Friedman, Ex officio.

Publication Committee: Harry Hauser, Chairman, Cleveland, Ohio; Wendell C. Hall, Hartford, Conn.; Martin Van Herik, Rochester, Minn.

Public Relations Committee: H. Peter Mueller, Chairman, Belmont, Mass.; Harold W. Jacox, New York, N. Y.; Charles H. Peterson, Roanoke, Va.

Janeway Lecture Committee: Edith H. Quimby, Chairman, New York, N. Y.; William S. MacComb, Houston, Tex.; Clifford L. Ash, Toronto, Ont.

Representatives on the American Board of Radiology: Frederick W. O'Brien, Boston, Mass.; Bernard P. Widmann, Philadelphia, Pa.; Donald S. Childs, Jr., Rochester, Minn.

Representatives on the National Committee on Radiation Protection: Robert Robbins, Philadelphia, Pa.; Herbert M. Parker, Richland, Wash.

Representative on the Board of Chancellors of the American College of Radiology: Milford D. Schulz.

Forty-sixth Annual Meeting: Greenbrier Hotel, White Sulphur Springs, W. Va., April 13–16, 1964.

EDITORIALS

THE SIXTY-FOURTH ANNUAL MEETING OF THE AMERICAN ROENTGEN RAY SOCIETY

THE Sixty-fourth Annual Meeting of the American Roentgen Ray Society was held at the Queen Elizabeth Hotel in Montreal, Province of Quebec, from Tuesday, October 8 through Friday, October 11, 1963. President Earl E. Barth called the meeting to order and introduced Councilor John Lynch-Staunton representing His Worship, the Mayor of Montreal, who extended a most cordial welcome to this bilingual city. Paul-Emile Coté, M.D., President-Elect of the Quebec Division of the Canadian Medical Association, then related numerous incidents referring to Canadian radiologic history and cited the two medical traditions which have existed in the past and continue to evolve side by side in Quebec. Hôtel Dieu is the oldest hospital in North America and McGill University has the longest history of uninterrupted bedside teaching in North America.

President-Elect Ralph M. Caulk, M.D., was then installed as President of the Society and Dr. John P. Medelman, Chairman of the Executive Council, awarded the President's Medal. The presentation of two gavels, one symbolic and the other working, immediately followed.

Dr. Caulk's Inaugural Address entitled, "On the Preservation of an Image," was most timely and exhorted radiologists to be eternally vigilant, impeccably honest and perpetually to strive for improvement. Above all else the clinical role of the radiologist should be engendered. Dr. Caulk's Inaugural Address is published in full in this issue of the JOURNAL.

The Scientific Session of the Society began immediately thereafter with presentation of ten papers devoted to mammography, angiography and certain aspects of neuroradiology. The last two papers of the morning were concerned with 2 mev. irradiation of lymphoma and an application of subtraction technique to tomographic systems.

Scientific papers were limited to the mornings, allowing time for the study of scientific and technical exhibits from lunch until 3:00 P.M. when instruction courses were convened. The scientific exhibits, the largest number to ever have been assembled by the Society under the enthusiastic and able chairmanship of Dr. Lewis E. Etter of Pittsburgh, are described elsewhere in this issue of the JOURNAL.

On Tuesday evening the Annual Caldwell Lecture was given by an eminent scientist, Professor Robert McWhirter, from Edinburgh, Scotland. Dr. McWhirter, Professor of Radiotherapy at the University of Edinburgh and Director of Radiation Services in the Royal Infirmary and Western General Hospital at Edinburgh, Scotland, titled his lecture, "Should More Radical Treatment Be Attempted in Breast Cancer?" and based it on his many years' work which has brought a most valuable contribution to the problem of breast cancer. He stated that "planned clinical trials should be organized so that the value of these more radical procedures may be tested and so that the best combination of surgery and radiotherapy may be determined." Professor McWhirter was introduced by President Ralph M. Caulk and was subsequently presented with the Caldwell Medal.

On Wednesday the Scientific Session was

comprised of thirteen papers, dealing with pulmonary problems, one with the larynx and the remainder with various problems of angiocardiography, principally cardiac lesions.

On Wednesday afternoon a panel discussion on the activities of the American College of Radiology was held with Dr. Ralph M. Caulk presiding, Dr. T. J. Wachowski, Moderator, and Dr. John D. Reeves, Dr. Ted F. Leigh, Dr. Earl E. Barth, Dr. W. D. Buchanan and Dr. David S. Carroll as panelists. This interesting and informative presentation was well attended and as in past years has afforded guidance particularly to younger radiologists through the multifaceted activities of the College.

On Thursday morning the scientific papers given concerned pharyngeal and esophageal perforations during endoscopic procedures, the thoracic duct, causes of rib notching, treatment of cancer of the esophagus, use of abdominal flat films as a survey procedure, hypovolemia resulting from water soluble contrast agents in children, radioisotope studies in the diagnosis of stomach lesions, evaluation of techniques for demonstrating duodenal ulcer craters, and radiologic findings in diseases of the lesser peritoneal sac. Four papers dealt with certain aspects of radiation therapy and radiobiology.

On Thursday evening the Annual Banquet was held with the announcement of the newly elected officers. Awards were presented for those scientific exhibits judged to be the best. A colorful stage show immediately followed and in turn was followed by a pleasant evening of dancing.

On Friday morning the diagnostic applications of closed circuit television in neuroroentgenology headlined a group of three papers dealing with modern techniques of television, television tape recording and image amplification. Other papers presented the problem of the remaining kidney in survivors of Wilms' tumor, cancer clinic experience in Ontario and *in vivo* radiation dosimetry. Four papers on certain aspects of urologic roentgenology followed and the usefulness of radiologic examination of the larynx in patients with squamous cell carcinoma concluded this Scientific Session.

The Director of Instruction Courses, Dr. Harold O. Peterson, assisted by Dr. Donn G. Mosser, organized a most interesting group of courses dealing with diagnosis, therapy and other pertinent radiologic topics. The number of technical exhibits, which were assembled under the direction of Mr. Clifford L. Sherratt, Honorary Member, and Dr. James C. Cook, Manager of the Annual Meeting, was very large. A list of the Technical Exhibitors is presented elsewhere in the JOURNAL.

The excellent attendance at the meeting was in part due to its location in beautiful Montreal, which, having more French speaking people than any other city of the world exclusive of Paris, holds a special charm for North Americans.

The Committee on Local Arrangements under the Chairmanship of Dr. Carleton B. Peirce and the Ladies Committee under the Chairmanship of Mrs. Carleton B. Peirce are to be congratulated on the excellent taste and efficient manner in which the ladies' activities were arranged. The golf widows' dinner and theater party on Monday hosted by Councilor McKenna, a city tour on Tuesday, Laurentian Mountains tour on Wednesday and a tour of the Botanical Gardens on Thursday were all enthusiastically attended and enjoyed by the ladies. The Society is deeply grateful to Mrs. Peirce and her Committee for having arranged this outstanding program.

The Annual Golf Tournament held at the Royal Montreal Golf Club on Monday afternoon was followed by an excellent dinner. The club remained open an extra day past its usual season to provide us with this most enjoyable day and delightful dinner.

The Queen Elizabeth Hotel is admirably arranged for a meeting of this type and provided a convenient grouping of meeting rooms, and scientific and technical exhibit space to permit the maximum utilization of information presented.

The Committee on Public Relations was chaired by Dr. Jean Bouchard who was capably assisted by Mr. Otha W. Linton and Mr. David G. Pettengill from the American College of Radiology.

Dr. Carleton B. Peirce, in particular, should be commended for his able Chairmanship of the Committee on Local Arrangements. A word of special gratitude is extended by the Society to His Worship, the Mayor of Montreal, and members of his Staff, particularly the Director of Parks and the Director of Catering Services.

President Caulk can be justifiably proud of the Sixty-fourth Annual Meeting, which was a grand success in every respect.

Kenneth L. Krabbenhoft, M.D.
Harper Hospital
Detroit 1, Michigan

* * *

SHERWOOD MOORE, M.D.
1880-1963

DEATH came to one of America's most beloved pioneer radiologists, Dr. Sherwood Moore, on Tuesday, July 9, 1963. He had just finished a telephone conversation with his son, Dr. Andrew Moore of Lexington, Kentucky, when he experienced an acute coronary thrombosis and died within a few minutes. Dr. Moore, born in Lynchburg, Virginia on October 28, 1880, was the son of a successful tobacco warehouse owner, Israel Sneed Moore, and his wife, Nellie Hayward Wise.

For two years he studied at the University of Virginia and later received his degree, Doctor of Medicine, from Washington University School of Medicine in St.

Louis in 1905. He interned at the St. Louis City Hospital from 1905 to 1906, and served as senior resident in obstetrics at Washington University Hospital from 1906 to 1907. He then joined his brother, Dr. Bernard Moore, who was engaged in the private practice of obstetrics and gynecology in St. Louis. When his brother died the following year, Dr. Malvern B. Clopton asked Dr. Moore to be his assistant in the practice of general surgery. From 1910 to 1913 Sherwood Moore served as Assistant in Surgery at the St. Louis Children's Hospital. It was during this period that he met the new Assistant Chief Nurse, Miss Veronica Mollison, who had just come from Boston's Children's Hospital to introduce their advanced methods of child care. Five years later she was to become Mrs. Sherwood Moore.

In 1914 he had the interesting experience of being the physician for the Union Minière Co. in the Belgian Congo. His work in Africa had intensified an interest in radiology that began when he was practicing obstetrics and surgery. At the end of the year, he returned to Richmond, Virginia, where he went for instruction in radiology under Dr. Alfred L. Gray. He remained with Dr. Gray for about one year and then went to Boston in 1916–1917 to be the first resident in radiology at the Massachusetts General Hospital under the famous Dr. George W. Holmes. While there he also came under the influence of Dr. Walter Dodd, one of the early martyrs in radiology.

On his return to St. Louis in 1917, Dr. Moore was appointed Assistant Professor in Surgery (X-Ray) at Washington University School of Medicine, and Roentgenologist to Barnes Hospital. In 1926 he was promoted to Associate Surgeon and in 1927 became one of the first Professors of Radiology in this country. In 1930 he was also made the Director of the Mallinckrodt Institute of Radiology. In these positions he served as the Radiologist to Barnes Hospital, the St. Louis Children's Hospital, the St. Louis Maternity Hospital, the Shriner's Hospital, and the McMillan Hospital, all affiliated with Washington University School of Medicine.

As an administrator he filled these positions with distinction and with an equanimity that characterized his leadership. Dr. Moore held firm beliefs and was guided by unequivocal principles. In carrying on his work, he was efficient but friendly. He possessed the ability to choose competent associates and to give them responsibility which he believed did more to develop young men than any other factor. He demanded their acceptance of these responsibilities and required their loyalty which he returned in full measure. The door to his office was always open to anyone seeking counsel on either professional or personal problems. He had a deep, gentle understanding and love for his friends and colleagues and his relations with them were always those of a Virginia gentleman. His years in private practice gave him an insight into the problems and uncertainties of the practitioners who consistently sought him for consultations.

As a teacher he had an abiding faith and affection for the young physician, the intern, the resident, or the doctor just starting his academic career or entering private practice. He thoroughly enjoyed the company and confidences of young people. He believed in learning through experience and by guiding the receptive mind, as opposed to regimentation and formal didactic lectures. As a teacher, he was at his best as a preceptor. This method of training young radiologists proved most productive for Sherwood Moore's "boys" who are scattered across the country in positions of importance in both academic radiology and in private practice.

Dr. Moore was a scholar of stature. By his schooling he was well grounded in the classics and humanities, and was facile in both Greek and Latin, as well as in German and French. His scientific writings were distinguished by a clear, direct, and concise style, and often lightened by an appropriate reference to Greek mythology. He was a prolific reader, and enjoyed old books, manuscripts, and first editions.

Dr. Moore was an effective blend of a physician and a scientist. He enjoyed most the informal consultations with his colleagues in the untangling of intricate diagnostic problems or in the determination of the method of treatment most applicable for a patient. He liked to see the patient and to visit with him in order to gain a clearer insight into his problems. He possessed an inquiring mind and a tenacious memory. His first interest, one that was to remain with him throughout his scientific career, was the study of bone, its complex physiology, its variations in growth, and the mechanisms by which disease transformed its architecture. In this field he became absorbed in the disorder of Hyperostosis Cranii, which resulted in a book of this title. Earlier, he and the late J. Albert Key, Professor of Clinical Orthopedic Surgery, translated from French into English the classic book by Lariche and Policard on "The Normal and Pathological Physiology of Bone: Its Problems."

The most productive decades of his life were the 1920's and 1930's when he worked with the late great Dr. Evarts A. Graham, then Professor of Surgery at Washington University School of Medicine, and his associates, Dr. Warren H. Cole and Dr. Glover H. Copher, in the development and perfection of cholecystography. In recognition of this superb achievement, he shared with them the Gold Medal of the St. Louis Medical Society.

As a result of the epochal success with cholecystography, Mr. Edward Mallinckrodt, Chairman of the Board of the Mallinckrodt Chemical Works, asked Dr. Graham to determine the most critical needs of the Medical School. At that time the Department of Radiology was "ill-housed" in cramped and antiquated quarters. Most of the equipment was obsolete and unequal to the exciting developments that were taking place in the diagnosis and surgical treatment of diseases of the chest. Dr. Graham knew that Dr. Moore and his associate, Dr. Walter Mills, wanted and urgently needed a new department and that they had even prepared tentative sketches and plans for an Institute of Radiology that would serve all of the affiliated hospitals in the Medical Center. It is to Dr. Graham's credit that he told Mr. Mallinckrodt about this project and recommended that it have high priority.

Dr. Moore was always looking ahead and so he was prepared for Mr. Mallinckrodt's decision to build the Institute—the first in this country. It has been affectionately referred to as the "House Cholecystography Built." When it was completed in 1930, only four of the eight floors could be filled, but today it is overcrowded. Dr. Moore had foreseen the remarkable advances and expansion that were to occur in radiology.

During this period Dr. Moore was working with Dr. Graham and Dr. J. J. Singer when they were building up the Chest Service which was to culminate in the first successful removal by Dr. Graham of an entire lung for carcinoma. The techniques of bronchography and roentgen kymography were introduced at this period, both of which he supported and aided in perfecting. These were followed by his construction of the Kieffer Laminagraph and his application of it to diagnostic roentgenographic examinations. For his part in these achievements and for his work on hyperostosis cranii, he received Honorable Mentions from the American Medical Association and the Canadian Medical Association in 1935; the Silver Medal of the American Academy of Orthopedic Surgeons in 1936; the Honorable Mention of the Southern Medical Association, and of the Fifth International Congress of Radiology in 1937; the Bronze Medal of the Mississippi Medical Society in 1938; and the first award of the Radiological Society of North America in 1939. He also received Certificates of Merit from the American Roentgen Ray Society and the American Medical Association in 1936, and from the latter again in 1939. All of these awards were received in recognition of his contributions to clinical research. In later years he supported the development of roentgenographic equipment for the rapid serial automization of x-ray exposures for cardiovascular and cerebral angiography. His total bibliography comprised nearly a hundred scientific papers, books, and contributions to books.

In the field of radiation therapy, Dr. Moore was the first to bring deep roentgen therapy equipment to the St. Louis area in the early 1920's. Together with Dr. D. K. Rose, Professor of Urology, and the late Dr. Ernest T. Sachs, Professor of Neurological Surgery, he investigated the effects of single massive doses of radiation on tumors exposed through the operative wound. His major interest, however, was the management of tumors about the head and neck, as evidenced by his co-authorship with the late Dr. Vilray P. Blair and Dr. Louis T. Byars of the book, "Cancer of the Face and Mouth."

Dr. Moore maintained an active interest in scientific and medical organizations and was a Fellow of the American College of Radiology and of the American Medical Association. He was a member of the Radiological Society of North America, the Southern Medical Association, the Missouri Medical Association, and the St. Louis Medical Society. He especially enjoyed the American Roentgen Ray Society whose meetings he regularly attended and by which he was honored by being made President in 1942. He derived considerable pleasure from his services as a member of the National Advisory Cancer Council of the American Cancer Society of which he was a Director-at-Large from 1948 to 1953. He was at home in the deliberations of committees and the governing boards of organizations and spoke freely of his mind. He enlivened many meetings with his wit and homey stories about the South.

In 1949, Dr. Moore was made Professor Emeritus of Radiology and he and Mrs. Moore retired to their farm in the Missouri Ozarks. They had developed this from a week-end place to a year-round home and spent the past ten years there. Dr. Moore was enthusiastic about outdoor life, and was especially familiar with the habitats of wild animals. Both Dr. and Mrs. Moore enjoyed entertaining their friends in their home, which was always done in a gracious and hospitable manner. Dr. Moore is survived by his wife; two sons, Dr. Andrew Moore, who is in the practice of plastic surgery at Lexington, Kentucky, and the Reverend Peter Moore, an Episcopal priest, Indianapolis, Indiana; two brothers, Maurice and Donald, and two sisters, Miss Eve Moore, and Mrs. N. C. Manson, all of Lynchburg, and nine grandchildren.

To the very end, Dr. Moore maintained an avid interest in radiology, in politics, and in furthering wild life conservation. In his passing, radiology loses an administrator of character, an inspiring teacher, an avid investigator, a noble physician, and a true friend of mankind.

Wendell G. Scott, M.D.

IN MEMORIAM
A. STANLEY KIRKLAND, M.D.
1890-1963

DR. A. Stanley Kirkland, dean of Radiologists in the Province of New Brunswick, died suddenly at his home, August 13, 1963, at the age of 73. He had been Head of the Department of Radiology at the Saint John General Hospital from 1922 until 1954 and, following his retirement from the service of Radiology, he spent a further five years in the general administrative work of the hospital. He was a distinguished member of the medical profession and contributed much to the New Brunswick and to the Canadian Medical Association.

Dr. Kirkland was born in Salem, Oregon, but the family moved when he was very young to Westminster, British Columbia, where he received his early education. He graduated from McGill University Medical school in 1913 and this was followed by postgraduate training in Surgery at the Montreal General Hospital. He enlisted in the Royal Canadian Army Medical Corps, where his interest shifted to Radiology, and he was attached to the First Canadian Casualty Clearing Station. With this Unit he became the first radiologist in the forward areas in France.

Following World War I, Dr. Kirkland joined the Staff of the Department of Radiology at his old hospital, the Montreal General, remaining there until his move to Saint John in 1922. He soon became very prominent in medical affairs on both the provincial and national levels. For many years he was Secretary of the New Brunswick Medical Society, was its President in 1930–1931, was made an honorary member at the age of 70, and continued active in committee work until the time of his death. In the Canadian Medical Association, Dr. Kirkland had served as the Provincial Representative on the Executive Committee and as a member of the Standing Committee on Radiology. For many years he represented the Province on the Medical Council of Canada, being elected President of this body in 1945–1946. He was also awarded Honorary Membership in the Canadian Medical Association and, many years prior to this, acquired his Fellowship in the Royal College of Physicians (Canada).

During the Second World War, Dr. Kirkland recruited the 14th Field Ambulance in Saint John. His age and his need by the community prevented his going abroad with this unit but he remained active in the training of reserve units, retiring in 1944 with the rank of Lieutenant-Colonel.

Dr. Kirkland is survived by his widow, also by a brother, Aubray, and a sister, Bessie, both of New Westminster, B. C.

Norman S. Skinner, M.D.

IN APPRECIATION

HARRY W. DACHTLER
Last Charter Member of the
American Roentgen Ray Society

HARRY W. DACHTLER

HARRY W. DACHTLER, pioneer in Roentgenology and the last of the self-educated roentgenologists, died in Toledo, Ohio, May 24, 1961.

Mr. Dachtler was born in Franklin, Ohio, September 22, 1871. He went to school in Franklin, where he never learned enough German to pronounce his own name correctly, but learned enough about electricity that he spent all of his spare pennies, even as a child, on batteries and electrical appliances. He also developed an interest in chemistry which continued until he all but blew himself up in an explosion of homemade gun cotton.

For a time he attended school in Cincinnati, where he worked in the practical application of electricity and in electrical engineering. In 1892 he came to Toledo. His first occupation here was as an accountant with the B. F. Wade Company. In 1895 came news from Germany of the discovery of the new kind of light, the invisible x-ray. From then on Mr. Dachtler spent less time in accounting, and more time in studying the invisible x-ray. He soon assembled an x-ray machine, the coil for which he wound himself, and started exposing x-ray plates—a full time roentgenologist. For many years, of course, he used glass plates. By 1900 he had advanced enough to help found the American Roentgen Ray Society in St. Louis. He was secretary of this Society at one time and at his death was the last surviving Charter Member.

Harry Dachtler had no formal education in roentgenology. Who was there to teach it in those days? He had no academic degree but went wherever he saw light, *the invisible light*—to Pancoast and Pfahler in Philadelphia, to Baetjer in Baltimore, to Schüller and Frankl in Vienna. He was always studying medicine on the side. Every two or three years he went to Europe to learn more.

Mr. Dachtler was one of the first to warn of the danger of overexposure to roentgen rays. While he lost a finger from repeated exposure, he suffered much less than many of his contemporaries.

In the early days x-ray literature was not as voluminous as it is today. Mr. Dachtler published only a few articles of general interest, but he was held in the highest regard and respect for his contributions all over the x-ray world of his time.

Harry Dachtler was an energetic, fearless personality. He loved many sports, was an excellent trap shot, dry fly fisherman, duck hunter, sailor, and swimmer. He always drove a fast automobile, sailed his boats in the worst weather, hunted canvasbacks in sleet storms, traveled on the fastest luxury liners, and loved a law suit.

In 1915, he was Roentgenologist to all four Toledo hospitals, but he always insisted on keeping a private office, apart from any hospital. As younger men came to Toledo, he gave up his hospital connections, but continued private practice to about 1948.

Until his death, Harry Dachtler was an ardent supporter of The American Roentgen Ray Society and one of its most distinguished members.

John L. Stifel, M.D.

THE SCIENTIFIC EXHIBITS

THE SCIENTIFIC EXHIBITS of the Sixty-fourth Annual Meeting of the American Roentgen Ray Society held at the Queen Elizabeth Hotel, Montreal, Quebec, Canada, October 8 to October 11, 1963 were by far the largest in number in the history of the Society. Dr. Lewis E. Etter, enthusiastic and untiring Chairman and his very able Committee on Scientific Exhibits spared no time or effort in assembling this most comprehensive visually documentative material which authoritatively supplemented the academic presentations of the Scientific Sessions. All Exhibits were of the highest technical quality and the Society, in its indebtedness, presented this year a Certificate of Appreciation to all Scientific Exhibitors for their immeasurable contribution to the success of the Annual Meeting. The Committee on Awards must have had the greatest difficulty in making the selection for the customary prizes. After thoughtful consideration a Bronze Medal and 11 Certificates of Merit were awarded. At this year's Meeting, through the initiation of Dr. Lewis E. Etter and his Committee, a Popularity Prize was also awarded. At the time of registration each registrant was supplied with a ballot, asking him to "Vote for the exhibit you like best." The happy winners of this contest were Dr. Giovanni Di Chiro and Mr. Joseph Morel of Bethesda, Maryland, who also received a Certificate of Merit for their outstanding exhibit.

The following is a description of the exhibits:

BRONZE MEDAL

Roentgenologic Evaluation of Nephrocalcinosis with Special Reference to Hyperoxaluria. Alfred L. Weber, M.D., Massachusetts General Hospital, Boston, Massachusetts.

Hyperoxaluria is one of several disease entities leading to nephrocalcinosis. A brief roentgenologic and pathologic description emphasized the most distinctive points.

This excellent exhibit dealt with nephrocalcinosis from the roentgenologic point of view. Many cases encountered at the Massachusetts General Hospital over a period of several years were analyzed and the 4 characteristic findings were presented in an attractive and most instructive form.

The important differential diagnostic features were also outlined.

Clinical and laboratory data supplemented the roentgenologic description.

CERTIFICATES OF MERIT

Urethrography in Children. R. Parker Allen, M.D., Edmund H. Burrows, M.D., and William S. Davis, M.D., Children's Hospital, Denver, Colorado.

This exhibit was based on experience with more than 1,000 patients who had voiding cystourethrographies and were cystoscoped.

The diseases found and the degree of cystoscopic correlation were given. Examples of normal variants as well as of the more common abnormalities were illustrated.

Emphasis was placed upon the diagnosis of urethritis in girls, showing some roentgen signs which have not been previously described.

Reversible Vascular Occlusion of the Colon. Scott Boley, M.D., Solomon Schwartz, M.D., Harvey Krieger, M.D., Kenneth Robinson, M.D., and Leon Schultz, M.D., Jewish Hospital of Brooklyn, Brooklyn, New York.

Clinical and experimental material was presented in this exhibit establishing reversible vascular occlusion of the colon as an entity and suggesting the possible relationship between vascular occlusion and ulcerative colitis.

The Vertebral Arteries—Positional Occlusion Post Mortem. B. L. J. Brown, M.B., B.S., and W. F. Tissington Tatlow, M.D. The Montreal General Hospital, Montreal, Canada.

In patients with cerebrovascular disorders, a group is recognized in which there is clinical evidence of ischemia of the brain stem. In this group, a few patients developed sudden attacks suggestive of ischemia, which coincided with certain positions of the head and neck in relation to the trunk. These attacks were rapidly relieved by return to neutral posture.

Postmortem vertebral arteriography on 41 subjects was done. Certain positions of the head on the neck produced temporary occlusion. The incidence of temporary occlusion was much higher when traction was applied to the head during positioning.

Multiplane Cineangiocardiography. Lucien Campeau, M.D., and Jacques Saltiel, M.D., Institute of Cardiology and Maisonneuve Hospital, Montreal, Canada.

A technique was presented permitting roentgenography in multiple successive planes by rotating a table to which an infant is firmly fastened. Satisfactory studies are obtained in the lateral, anteroposterior and in all the intermediate oblique planes, following a single injection of contrast medium. This technique has thus far been found useful in over 30 cases of congenital heart disease in infants.

Examples of cases of tetralogy of Fallot, pseudotruncus, transposition of the great vessels, pure pulmonic stenosis, stenoses of the pulmonary arteries, hypertrophic subvalvular aortic stenosis, atrioventricular canal and coarctation of the aorta were beautifully illustrated.

Axial Transverse Encephalography. Giovanni Di Chiro, M.D., and Joseph Morel, R. T., National Institutes of Health, Bethesda, Maryland.

This exhibit was intended to illustrate the technique and the results of axial transverse encephalography. A facsimile of the actual roentgenographic equipment used for the procedure was shown in rotating action. A dummy demonstrated how the patient is positioned to obtain the axial transverse laminagrams of the head after intrathecal injection of air.

An automatic projector showed the axial transverse encephalograms at the various levels.

This exhibit also won the "Popularity Prize."

Tumors of the Thymus—Roentgen Considerations. H. Gilmore Gregg, M.D., Kent Ellis, M.D., and Raffaele Lattes, M.D., Columbia Presbyterian Medical Center, New York, New York.

The roentgenographic manifestations of more than 65 tumors of the thymus gland were described and illustrated. Particular attention was given to the problem of the thymomas associated with myasthenia gravis. The relationships between thymomas and several interesting clinical syndromes were presented, and some important endocrinologic responses of the thymus gland were demonstrated.

History of American Radiology. E. R. N. Grigg, M.D., Cook County Hospital, Chicago, Illinois.

A retrospective glance into the radiologic past always furthers the understanding of current problems in the specialty. Three great stages are recognized: (1) The Era of the Roentgen Pioneers, (2) The Golden Age of Radiology, and (3) The Atomic Phase. The two World Wars were more than chronologic dividers of these stages.

This synoptic (*i.e.*, inherently incomplete) exhibit of skillful presentation included the men, apparatus and organizations regarded as more characteristic for each of the three stages in the History of American Radiology.

Selective Visceral Arteriography. Mordecai Halpern, M.D., and John A. Evans, M.D., The New York Hospital—Cornell Medical Center, New York, New York.

Visceral arteriography is in a stage of clinical investigation. Its application for preoperative diagnosis was presented as a step in evaluating the method's practical value. The detailed vascular anatomy and pathology of the visceral organs were shown since the preliminary results proved encouraging.

Dissecting Aneurysms of the Thoracic Aorta: Their Angiocardiographic Demon-

stration. Samuel D. Hemley, M.D., Virginia Kanick, M.D., Richard D. Kittredge, M.D., and Nathaniel Finby, M.D., St. Luke's Hospital, New York City, New York.

Ten cases of a total of 15 cases of dissecting aneurysm of the thoracic aorta studied during the last 24 months were presented with angiocardiograms, surgical and pathologic material.

The conclusion was reached that dissection of the thoracic aorta, particularly of the chronic type implying natural re-entry, is far more common than hitherto appreciated.

Although conventional roentgen studies may raise a high level of suspicion, the ultimate diagnosis prior to surgery rests with the contrast demonstration of the false channels, increase in the thickness of the aortic wall and decrease in the size of the aortic lumen. Intravenous angiocardiography is the safest and most practical method of study.

Premature Craniosynostosis. John A. Martin, M.D., Franklin L. Angell, M.D., and Edgar N. Weaver, M.D., Roanoke, Virginia.

This exhibit demonstrated premature closure of the sutures in craniosynostosis of infants with colored photographs and roentgenograms before and after surgery, and with ceramic casts of infants' heads before operation.

Technology of Radiation Therapy. Bernard Roswit, M.D., Harold Jones, M.D., Stanley Malsky, Ph.D., Cyprian Reid, B.Sc., and Louis Maddalone, Bronx Veterans Administration Hospital, Bronx, New York.

This exhibit has served well in the training of more than 100 resident and graduate radiologists in the technology of modern radiation therapy.

The student is indoctrinated, step by step, in a system of techniques designed to deliver radiation to the tumor with maximum skill and precision, while minimizing the risk to the patient and his normal tissues. Recent advances in general concepts, equipment, instrumentation and radiography are utilized to maximum advantage for tumor localization, treatment planning, mold technology, portal verification, *in vivo* dosimetry and for the radiation protection of the patient, technician and physician.

An exhibit manual was provided.

Other Excellent Exhibits Were:

Unusual Syndromes of Carcinomatosis. L. Reed Altemus, M.D., Presbyterian-University Hospital, Pittsburgh, Pennsylvania.

Three unusual "syndromes" of carcinomatosis were presented. They consisted of (1) osteosclerosis with extramedullary hematopoiesis; (2) pulmonary hypertension secondary to tumor embolization of the lung; and (3) the pseudo-Addisonian heart represented by a small cardiac silhouette, resembling the small heart seen with adrenal cortical insufficiency.

Angiographic Characteristics of the "Subclavian Steal" Syndrome. Robert N. Ashby, M.D., Bill G. Karras, M.D., and Abram H. Cannon, M.D., Chicago Wesley Memorial Hospital and Northwestern University Medical School, Chicago, Illinois.

The "subclavian steal" syndrome is a term used to describe the collateral filling of an occluded subclavian artery by reversal of flow in the ipsilateral vertebral artery.

This exhibit demonstrated the angiographic findings in several cases of the syndrome, and included several drawings showing the various anatomic pathways of collateral flow to an occluded subclavian artery. The angiographic techniques most suitable for visualizing the lesion were detailed.

The possible serious effects of the diversion of blood from the basilar artery, especially in the presence of concomitant cerebrovascular impairment, was emphasized, as was the rapidly increasing frequency of diagnosis.

Arthrography of the Knee. Ralph C. Aye, M.D., Thomas W. Dorr, M.D., and Garth

R. Drewry, M.D., Tampa General Hospital, Tampa, Florida.

Arthrography of the knee is a simple, safe and worth-while procedure that can be performed equally well by the radiologist in his office or in a hospital.

The procedure consists of the injection of a water soluble opaque material which outlines the menisci, articular surfaces of the femur and tibia, and the cruciate ligaments. The correct diagnosis of an injury to the knee can sometimes be made only by this procedure.

During the past 4 years arthrograms of 122 knees have been obtained by the exhibitors, all but 10 of these in their offices. Slightly more than one-third of the cases have been operated on. The diagnostic accuracy was 85 per cent.

Arthrography of the Knee. Raymond Belanger, M.D., Louis-Joseph Papineau, M.D., C. Charest, M.D., and M. Dufresne, M.D., Notre Dame Hospital, Montreal, Canada.

The technique of serial meniscography was demonstrated.

This technique consists mostly of spot roentgenography under visual control. Many typical meniscal lesions as well as other pathologic conditions of the knee joint were illustrated.

Clinical pathologic studies and statistical data were also presented.

Hirschsprung's Disease in Infancy. Walter E. Berdon, M.D., and David H. Baker, M.D., The Babies Hospital, Columbia-Presbyterian Medical Center, New York, New York.

Hirschsprung's disease is a lesion of early infancy. Not readily diagnosed, it leads to mortality figures approaching 50 per cent.

The points of the earliest possible diagnosis were stressed, including recognition of atypical forms such as total colonic and small bowel involvement. The lethal complication of enterocolitis and its diagnosis were also considered.

Transhepatic Percutaneous Cholangiography. M. Paul Capp, M.D., Clarence E. Gardner, M.D., R. J. Flemma, M.D., and R. J. Reeves, M.D., Duke University Medical Center, Durham, North Carolina.

Transhepatic percutaneous cholangiography is invaluable in patients with jaundice of obscure etiology and in postoperative biliary surgical patients without jaundice but with signs and symptoms of cholangitis. Extrahepatic obstruction can be differentiated from intrahepatic disease.

This exhibit was based on experience with 60 cases, 7 of which were spared operation because the diagnosis of intrahepatic hepatitis was correctly made. The accuracy of diagnosis is 90–95 per cent.

Characteristic roentgenographic findings were observed in 16 of 18 cases of carcinoma of the pancreas.

Case of the Day. Department of Radiology, The Montreal General Hospital, Montreal, Canada.

In this exhibit an unusual "case of the day" was presented with all pertinent data of information for the diagnostic acumen of the visiting participants.

Pneumothorax and Pneumomediastinum in the Newborn. Charles N. Chasler, M.D., University of Pittsburgh Medical School—Magee Women's Hospital, Pittsburgh, Pennsylvania.

There were approximately 80,000 deliveries at Magee Women's Hospital from 1948 to 1962. The roentgenograms and charts for this period were studied and 35 cases of pneumothorax and/or pneumomediastinum were encountered.

These cases were reviewed and the findings were presented in the exhibit in a tabularly arranged form. Clinical data were included and the specific roentgen features were illustrated with the aid of multiple roentgenograms. The differential diagnosis and treatment were also considered in detail.

Cranial Vessels—A Teaching Exercise. Lois C. Collins, M.D., Robert D. Heilman, M.D., and Priscilla J. Gibbs, B.A., Baylor University College of Medicine, Houston, Texas.

A method was presented of teaching cerebral circulation (arterial and venous) by assembling a three dimensional model from contents of a locally constructed kit consisting of: (1) plastic replica of the base of skull; (2) colored wires representing arteries and veins; and (3) a clear plastic falx.

This exercise permits a spatial appreciation of the vessels and correlation of their positions with the cerebral fissures and cisterns.

Azygography in the Evaluation of Operability of Pulmonary Carcinoma. Jack R. Dreyfuss, M.D., David B. Skinner, M.D., Murray L. Janower, M.D., and George L. Nardi, M.D., Massachusetts General Hospital, Boston, Massachusetts.

Venous azygography has been used for the specific purpose of assessing operability of pulmonary carcinoma.

The results of over 100 examinations were presented together with directions for utilizing two techniques of controlled injection, spot-film fluoroscopy and Polaroid roentgenography.

Mammography. Robert L. Egan, M.D., Methodist Hospital, Indianapolis, Indiana.

The technique of mammography was described. Data on radiation exposure to the patient were given.

The appearance of normal, benign and malignant conditions of the breast was outlined. The results of 24 institutions participating in a reproducibility study of mammography, of numerous radiologists using the technique, and of the exhibitor were presented.

Observations on Retrograde Vertebral Blood Flow. Romeo Ethier, M.D., Montreal Neurological Institute, Montreal, Quebec, Canada.

Angiography has recently disclosed reversal of blood flow in either vertebral artery. Demonstration of such a condition has cast a new light on the interpretation of complex neurologic syndromes associated with decreased blood pressure in the arm, ipsilateral to the reversal of the vertebral blood flow.

In the past 2 years, 4 patients presenting this condition, which is better known as the "subclavian steal or vertebral steal syndrome," were observed by the exhibitor.

Collateral circulation other than retrograde vertebral blood flow was also discussed.

Ego-D-Flater V: Benign Lesions of Bone. John H. Feist, M.D., Robert N. Berk, M.D., and Richard Granke, B.S., Presbyterian University Hospital, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.

An automatic testing and grading device, previously utilized to demonstrate important anatomic areas, illustrating now the possibility of errors in the roentgen diagnosis based on gross morphology alone, on the subject of benign tumors of bone, was presented.

Volume Characteristics of the Left Heart Chambers in Mitral Valve Disease. Melvin M. Figley, M.D., Tamnit Ansusinha, M.D., William J. Mikkelsen, M.D., Robert A. Bruce, M.D., and John B. Blackmon, M.D., University of Washington, Seattle, Washington.

Biplane angiocardiography permits observation of cyclic changes in the volume of the left atrium and ventricle expressed relatively (Soloff, Figley) or in absolute units (Arvidsson, Chapman, Dodge).

A study of patients with mitral valve disease using the most accurate method, the Dodge method, has permitted calculation of diastolic emptying rates of the left atrium and filling rates of the left ventricle. On this basis, the impediment in mitral stenosis may be differentiated from mitral incompetence and expressed numerically. From contemporary flow and pressure studies, mitral incompetence may also be expressed numerically—as a fraction of left ventricular stroke volume. These same data provide another means of calculation of the effective mitral orifice.

The principles involved and results obtained in approximately 35 intensively studied patients were presented.

Percutaneous Retrograde Femoral Aortog-

raphy. Abraham Geffen, M.D., and Maurice Goodgold, M.D., Beth Israel Hospital, New York, New York.

This exhibit showed that percutaneous retrograde femoral aortography is practical for a moderate sized hospital in routine diagnostic problems.

The following conditions were demonstrated: hypertension with primary renal arterial disease (fibromuscular hyperplasia, atherosclerosis) and aortic and iliac artery atherosclerosis; renal cyst versus neoplasm; renal artery aneurysm; congenital anomalies of kidney and renal vessels; inflammatory and obstructive renal lesions (hydronephrosis, tuberculosis, pyelonephritis); metastatic lesions of liver and adrenal; and retroperitoneal lesions.

Autothermographic Radiography. J. Gershon-Cohen, M.D., S. M. Berger, M.D., A.-G. B. Borden, M.D., and J. D. Haberman, M.D., Albert Einstein Medical Center, Philadelphia, Pennsylvania.

The theory, apparatus and practice of autothermography were detailed and exhibited, demonstrating the diagnostic range of this new discipline.

Comparative roentgenography will reveal the value of thermography in the solution of a wide spectrum of diagnostic problems.

Subtraction Technique in Head and Neck Angiography. William Hanafee, M.D., Paul Stout, and William Weidner, M.D., University of California Medical Center, Los Angeles, California.

The subtraction technique is a photographic method of eliminating the confusing shadows of superimposed bone. A more accurate appraisal of the extent and blood supply of head and neck tumors can be made utilizing the subtraction technique especially when angiograms have been obtained by the selective catheter technique.

Mammography. Laurent Huot, M.D., and Pierre Perras, M.D., Hôpital Jean-Talon, Montreal, Canada.

The help provided to physicians by this method has been revived. The exhibitors showed examples encountered in everyday practice. The equipment and technique were described in detail.

Lymphangiography—A Critical Evaluation. P. R. Koehler, M.D., George T. Wohl, M.D., Burton Schaffer, M.D., and Wayne Meyers, M.D., Philadelphia, Pennsylvania.

This exhibit illustrated the results, limitations and complications of lymphangiography. Pathologic-roentgenologic correlation in over 50 patients was presented. Experimental work concerning the spread of tumor cells using this procedure and the distribution of ethiodol in the body were briefly discussed.

Biplane Gastroduodenal Examination: A New Approach Using the Effect of Gravity on Mobility. Harold M. Landsman, M.D., and Howard J. Barnhard, M.D., University of Arkansas Medical Center, Little Rock, Arkansas.

Multiple projections are considered essential for most roentgenologic examinations. This point is especially recognized for the stomach and duodenum. Virtually ignored, however, is the fact that the extreme mobility of the stomach in response to gravity makes exact comparison from view to view impossible. The commonly used prone and right-side-down lateral views do not provide a correlatable biplane study.

Series of matched right-angle pairs of roentgenograms made in different positions were presented to demonstrate: (a) the normal anatomy for different body types, and (b) their value in the diagnosis of abnormalities, and particularly extragastric masses.

Pharyngeal and Esophageal Perforations during Instrumentation. Ted F. Leigh, M.D., and James L. Achord, M.D., Emory University School of Medicine, Atlanta, Georgia.

Pharyngeal and esophageal perforations may occur inadvertently during examinations with a variety of instruments, including the esophagoscope, gastroscope, fiberscope, and dilators. The clinical findings are determined by the level of the perforation and its effect on the surrounding structures. Atypical clinical findings are not uncommon, and a high index of suspicion must be maintained. Emergency roentgenologic studies should be undertaken immediately in suspected cases.

Representative examples were presented and authoritatively discussed.

Changes in the Anterior Choroidal Artery in Intracranial Lesions. Marjorie Le May, M.D., David Jackson, M.B., B.S., and John H. Drew, M.D., Boston VA Hospital, Tufts Medical School, Boston University School of Medicine, Boston, Massachusetts.

The anterior choroidal artery is readily identified in most cerebral arteriograms, especially if serial films or stereoscopic projections are used. The size and course of the artery provide valuable, and often decisive, diagnostic information.

Examples were given of the characteristic appearance of the artery in normal people; in patients with neoplasms and other affections of the temporal lobe; masses elsewhere in the brain; uncus herniation; and insufficiency of the basilar artery.

Gynecologic Patterns in Lymphography (Diagnosis and Therapy in Cancer). Edwin J. Liebner, M.D., and Peter Siegel, M.D., University of Illinois Research and Educational Hospital, Chicago, Illinois.

This exhibit gave a presentation of the lymphangiographic technique and a résumé of the experiences of the exhibitors in over 40 gynecologic patients exemplifying patterns in cervical, vulvar and other gynecologic cancers.

Besides these patterns, clinical therapeutic application utilizing a radioactive isotope based on earlier animal studies was also considered.

A final summary and appraisal of the value of the method were made.

Cobalt 60 Radiographs—Technical Factors. Leonard M. Liegner, M.D., and Norman J. Michaud, B.S., St. Luke's Hospital, New York, New York.

The response of Medical Screen and Industrial Type X-Ray films to cobalt 60 gamma radiation was presented. "Characteristic" curves have been constructed for different film types based on film dosimetry studies for films exposed in cardboard or bakelite cassettes, with and without lead and/or phosphor intensifying screens. The validity of these characteristic "curves" in providing accurate parameters assuring reproducibility of quality radiographs was amply demonstrated by a display of cobalt 60 chest radiographs.

A derived exposure factor chart permits interchanging of film type, intensifying screens and cassettes to obtain radiographs of desired contrast and definition dependent upon exposure variable.

An analysis was offered of the relative contributions in image production of the gamma photons, light photons and electrons emitted from the lead intensifying screen as they interact with the film emulsion.

The Spalteholz Skull. Jesse T. Littleton, M.D., and Lewis E. Etter, M.D., The Robert Packer Hospital, Sayre, Pennsylvania, and Western Psychiatric Institute, University of Pittsburgh, Pittsburgh, Pennsylvania.

This exhibit showed a demineralized skull prepared by the famous anatomist Spalteholz in Leipzig, Germany, about 1920 and brought to this country by the late Gustav Bucky.

The specimen is enclosed in a large glass sphere containing methyl salicylate and the roentgen anatomic features of the skull are illuminated by light from a fluorescent panel in back of it.

Polydirectional Body-Section Roentgenography through Plaster Casts. J. T. Littleton, M.D., C. L. Rumbaugh, M.D., and F. S. Winter, M.D., Guthrie Clinic Ltd., The Robert Packer Hospital, Sayre, Pennsylvania.

The distinct advantage of pluridirectional body-section roentgenography in visualizing osseous structures through plaster casts and metallic fixation devices was demonstrated.

Scout Film Diagnosis of Abdominal Abscesses. Leon Love, M.D., and Robert Tuttle, M.D., Cook County Hospital, Chicago, Illinois.

A series of cases was presented in which the diagnosis of abdominal abscesses was made on plain roentgenograms of the abdomen. The important roentgenologic findings were pointed out and the various types as to their origin were discussed.

Direct Percutaneous Noncatheter Brachial Angiography. Thomas R. Marshall, M.D., J. T. Ling, M.D., Raul C. Gonzalez, M.D., and A. Hatam, M.D., University of Louisville School of Medicine, Louisville, Kentucky.

Cerebral, thoracic and abdominal angiography by a new method of direct noncatheter left and right brachial angiography was presented. The technique was demonstrated with the aid of drawings and an explanation of the method was given. The exhibitors' experience in over 200 patients was discussed.

No fatalities had occurred and the complication rate had been extremely low.

Postbulbar Duodenal Ulcer. William T. Meszaros, M.D., Hildegarde Schorsch, M.D., and Franz Gampl, M.D., Cook County Hospital and Illinois Masonic Hospital, Chicago, Illinois.

The postbulbar ulcer is important because of the high incidence of bleeding and because this lesion is often overlooked.

Illustrative cases were presented and the problems in diagnosis were discussed.

Neuroblastoma. William J. Miller, M.D., Hooshang Taybi, M.D., and John A. Campbell, M.D., Indiana University School of Medicine, Indianapolis, Indiana.

This exhibit presented the roentgen features in 48 patients with neuroblastoma. A wide range of roentgenographic findings in the abdomen, chest and skeleton was illustrated. The clinical manifestations and therapeutic results were briefly summarized.

Functional Hepatography. Augusto Moreno, M.D., Francis Ruzicka, M.D., L. M. Rousselot, M.D., Albert Burchell, M.D., S. F. Slafsky, M.D., and Jean Burke, A.B., St. Vincent's Hospital of New York City, New York, New York.

This exhibit concerned the development of a method of intrahepatic parenchymal deposition of contrast material and its use in small and large laboratory animals, in normal human subjects, in patients with hepatic cirrhosis and in patients with congestive heart failure.

The venous and lymphatic outflow mechanisms were demonstrated.

Retrograde Brachial Arteriography. Frederick Murtagh, M.D., Michael Scott, M.D., Marc S. Lapayowker, M.D., and Robert Baird, M. D., Temple University Medical Center, Philadelphia, Pennsylvania.

The neurosurgical and roentgenologic techniques of retrograde brachial arteriography were presented. The use of the open method with cannulation of the artery and percutaneous puncture without the use of a catheter were illustrated.

The roentgenographic results in 98 cases were shown with roentgenograms of representative cases.

Autotomography. Paul F. J. New, M.D., and Edward W. Webster, Ph.D., Massachusetts General Hospital, Boston, Massachusetts.

Autotomography is simple to perform and has proven to be a valuable adjunct to standard lateral projections in cerebral pneumography and in roentgenography of certain osseous structures.

The geometric factors involved have been explored in detail and the results obtained, which were given in this exhibit, indicate that precise technique will increase the value and reliability of the method.

Collateral Circulation Associated with Proximal Subclavian Artery Occlusion. Thomas H. Newton, M.D., University of California Medical Center, San Francisco, California.

Occlusion or stenosis of the proximal subclavian artery is a common finding in patients with symptoms of cerebral vascular insufficiency.

Angiographic studies performed in 150 patients demonstrated marked occlusion or stenosis in 20 per cent. The distal subclavian artery may be supplied by one or several collateral pathways. The vertebro-vertebral pathway is the most common and potentially the most dangerous since it diverts blood away from the brain.

Several other collateral pathways arising from the external carotid artery, thyrocervical trunks, or internal mammary arteries have been noted and were exhibited.

Transorbital and Chaussé III Techniques for Middle Ear Examination. Pierre Perras, M.D., and Guy Duckett, M.D., Hôpital Jean-Talon, Montreal, Canada.

Transorbital and Chaussé III techniques, which were presented in this exhibit, are excellent for visualization of the middle ear and antrum. The diagnosis of cholesteatoma is simplified.

These techniques are complemented by laminagraphy and magnification for precision work.

Roentgenologic Aspects of Schistosomiasis of the Urinary Tract. Philippe F. Polani, M.D., Veterans Administration, Outpatient Clinic, Washington, D. C.

Plain roentgenograms showing the specific alterations in the urinary bladder, the ureters and the renal calyces were exhibited.

Other roentgenograms demonstrated the correlation between schistosomiasis haematobium, also called bilharziasis, and urinary lithiasis. Intravenous pyelograms usually reveal extensive involvement of the entire urinary tract with resulting impairment of renal function.

Combined Selective Arteriography of Celiac Axis and Superior Mesenteric Artery. Klaus Ranniger, M.D., The University of Chicago, Chicago, Illinois.

Catheterization of the celiac axis and the superior mesenteric artery using Seldinger's percutaneous method is technically easy to perform.

Because of the extreme variability of the normal anatomic distribution of both vessels, and the interconnections between them, simultaneous angiography of both arteries, using two catheters, has been helpful in the diagnosis of masses in the upper abdomen and prior to selective infusion therapy in patients with metastatic disease.

The Talar-Tilt Angle. Gustav Rubin, M.D., Morris Witten, M.D., and David E. Ehrlich, M.D., U. S. Veterans Administration Outpatient Clinic, Brooklyn, New York.

The normal range of tilt of the talus in the ankle mortise was determined, permitting interpretation of the significance of this measurement in evaluating instability. The device employed for the production of Talar-Tilt was specially constructed to produce equal inversion stress on both ankles at the same time. This was illustrated.

Plesiosectional Tomography of the Ossicles. André Sansregret, M.D., Hôpital Maisonneuve, Montreal, Canada

The purpose of this exhibit was to demonstrate that precise tomography of the ossicles, formerly reserved to departments equipped with the "Polytome," is now within the reach of everyone, equipped even with the attachment type of tomograph.

The technique was described and the results were shown in normal cases as well as in chronic inflammatory reactions, cholesteatoma, congenital malformations, and traumatic dislocation of the ossicles.

The Layering and Jet Stream Effect of Contrast in Aneurysms and Blood Vessels. Mannie M. Schechter, M.D., and Milton Elkin, M.D., Albert Einstein College of Medicine, New York, New York.

The basic principles of mixing fluids of different densities were demonstrated both in the test tube and in the intracranial vasculature. The roentgen appearance of a stream of unopacified and opacified blood matter producing the jet stream effect was described.

Cinematography has also been used to illustrate this.

Pulmonary Sarcoidosis; 2–16 Year Serial Observations. Hildegarde Schorsch, M.D., Gertrude Engbring, M.D., Bernice Perdziak, M.D., Edward A. Piszczek, M.D., and Hyo Hyun Byun, M.D., Cook County Hospital, Stritch School of Medicine, Suburban Cook County Tuberculosis Sanitorium District, Chicago, Illinois.

A clinical summary and serial roentgenographic studies of pulmonary sarcoidosis showing the various types, transition from one type to another, regression, progression and complications were presented.

Postbulbar Duodenal Ulcer. Wendell P. Stampfli, M.D., and Howard E. Wilson, M.D., St. Luke's Hospital, Denver, Colorado.

Peptic ulcers distal to the duodenal bulb may behave differently from ulcers of the bulb itself. Their presence is associated with a distinct clinical problem, and their proper roentgenographic evaluation is difficult. Especially interesting is the occasional association of these ulcers with a defect which can be misinterpreted as duodenal neoplasm. This was demonstrated.

Mammography. The Importance of Technical Factors. Leonard Stanton, M.S., David A. Lightfoot, B.S., John E. Cullinan, R.T., Kenneth A. Soll, M.D., and J. Stauffer Lehman, M.D., Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania.

Technical factors greatly affect both the useful information and patient dosage in mammography. Adequate contrast and detail are essential to permit detection of minute calcific and soft tissue changes.

In this study, over 1,500 exposures were made of a breast phantom, varying kilovoltage and filter, target film distance and focal spot, as well as basic film types. The effect of using screens and grids was also determined.

The results were summarized and demonstrated with the aid of roentgenograms of two proven breast carcinomas.

The Normal Female Breast and Its Variations in Mammography. Philip Strax, M.D., and Maurice M. Pomeranz, M.D., City Hospital at Elmhurst, Elmhurst, New York, New York.

The breast is a dynamic structure strongly influenced by age, sexual development and endocrine glandular status. There are wide variations in size and structural elements as seen on soft tissue mammograms in apparently normal women. Mammograms of 3,000 women were classified into 4 groups: Adolescent, Mature, Involutional and Atrophic with subheadings for variations in amounts of glandular, fibrous and fatty elements. Although age is an important factor, over 20 per cent varied markedly from the expected type according to age. Study of normal variations should serve as a basis for determination of the abnormal.

Rib Notching: Its Many Causes. Byron E. Swenson, M.D., Max L. M. Boone, M.D., and Benjamin Felson, M.D., Cincinnati General Hospital, College of Medicine, University of Cincinnati, Cincinnati, Ohio.

There are over a dozen clinical conditions with which rib notching may be associated. The most frequent underlying mechanism is widening and redundance of intercostal arteries serving as collateral pathways in a variety of circulatory abnormalities. Dilated intercostal veins and intercostal nerve tumors may produce identical rib changes.

This exhibit demonstrated a number of the conditions causing rib notching, grouped according to the anatomic structure and pathologic alteration responsible for the notching.

A Laminagraphic Study of Hepatic Metastases. R. W. Talley, M.D., A. K. Poznanski, M.D., and D. J. Heslin, M.D., Henry Ford Hospital, Detroit, Michigan.

The thorium dioxide hepatogram as evaluated by laminagraphy is a useful aid in determining the status of hepatic metastases, with diagnostic, prognostic and therapeutic implications. The major value of this procedure has been in estimating the response of hepatic metastases to endocrine or chemotherapeutic treatment in patients with disseminated carcinomatosis.

The exhibit demonstrated that gross pathologic specimens correlated well with the roentgenographically visualized metastases.

Congenital Supravalvular Aortic Stenosis and Associated Pulmonary Vascular Anomalies. H. Taybi, M.D., E. L. Petry, M.D., A. D. Merritt, M.D., C. Palmer, Ph.D., C. H. Helmen, M.D., and J. A. Campbell, M.D., Indiana University Medical Center, Indianapolis, Indiana.

Supravalvular aortic stenosis is a relatively rare congenital anomaly. The combination of supravalvular and peripheral branch stenoses of the pulmonary arteries may be more frequent than has been reported.

In this exhibit the clinical, genetic, laboratory and roentgenologic aspects of 9 cases of supravalvular aortic stenosis were presented. In 6 of these, peripheral pulmonary stenosis was also demonstrated. The value derived from both right and left cardiovascular contrast studies was shown.

Transtracheal Catheter Bronchography. Arch W. Templeton, M.D., St. Louis, Missouri, and Claude E. Fendley, M.D., Memphis, Tennessee, U. S. Naval Dispensary, Norfolk, Virginia.

A technique for performing bronchography using a 14 gauge Intracath venopuncture needle and opaque catheter was presented. The needle and radiopaque catheter are introduced into the trachea through the cricothyroid ligament and the needle immediately withdrawn. The soft catheter allows complete freedom in positioning the patient.

Excellent bronchograms were obtained using 2 to 3 cc. of 1 per cent lidocaine intratracheally. There was no significant patient discomfort or serious sequelae. The examination was done on an outpatient basis.

Action of Vital Bone Substance in Bone Regeneration and Repair. Furman H. Tyner, M.D., and E. J. Tucker, M.D., Houston, Texas.

This exhibit presented the results of a 5 year research and clinical evaluation. Included were: color prints of assay, photomicrographs and experimental animals; tabulation charts; and roentgenograms of experimental and clinical studies.

The clinical evaluation was based on 354 cases, constituting a wide variety of bone pathology, from the combined effort of 15 individual investigators.

Mucosal Folds of the Upper Urinary Tract. Jean A. Vezina, M.D., L. P. Léger, M.D., O. Raymond, M.D., and Roland Guy, M.D., Hôpital du Sacré Coeur, Montreal, Canada.

An interesting roentgenologic observation of longitudinal mucosal folds in the upper urinary tract was illustrated with the aid of several cases.

Colored transparencies of some operative specimens accompanied the roentgenograms as well as the histologic material of 4 cases.

It was stressed that a urinary infection is frequently associated with this condition.

Roentgenologic Observations on the Lesser Peritoneal Sac. Lewis A. Walker, M.D., and H. Stephen Weens, M.D., Emory University School of Medicine, Atlanta, Georgia.

This exhibit illustrated the pertinent anatomic features of the lesser peritoneal sac and demonstrated the varying roentgenologic appearances encountered in diseases affecting this compartment of the greater peritoneal cavity.

Roentgenography of the Breast in Cancer Detection. John N. Wolfe, M.D., Richard S. McCaughey, M.D., and Bernard S. Kalayjian, M.D., Woman's Hospital, Yates Cancer Clinic, Wayne State University, Detroit, Michigan.

Twenty-five hundred women over 45 years of age who were examined at a Cancer Detection Center and found to have normal breasts were roentgenographed routinely. The group included all social and economic strata of the Detroit Metropolitan area.

The mammograms were interpreted as normal; benign diseases; and malignant lesions. The malignancies were graded 1, 2 and 3 on the basis of roentgenographic evaluation. The characteristics of the malignant tumors were different in some respects from those which were routinely detected by physical examination.

The results of this study were presented.

THE TECHNICAL EXHIBITS

THE TECHNICAL EXHIBITS of the Sixty-fourth Annual Meeting of the American Roentgen Ray Society, held at the Queen Elizabeth Hotel, Montreal, Quebec, Canada, October 8 to October 11, 1963, exceeded all previous records in volume and excellence. The ultramodern facilities of the luxurious hotel, with a specially designed Convention Floor providing spacious Exhibit Halls in the immediate vicinity of the Grand Salon where all the Scientific Sessions were held, were particularly pleasing features. They constituted a most inspiring background for the artistic display of the many important advances of the present day and future technical developments. The individual exhibitors availed themselves of this opportunity by introducing to the large number of visitors a dazzling array of new diagnostic, therapeutic and scintiscanning apparatus, all types of accessories, new contrast media and processing chemicals, high resolution systems for monochrome and color television radiology, new cineradiographic cameras and projectors, the latest books, monographs and other publications, and many other items of immeasurable interest to the radiologist.

Mr. Clifford L. Sherratt, Honorary Member, and Dr. James C. Cook, Manager of the Annual Meeting, as usual, contributed greatly to the organization of the Technical Exhibits, thereby enhancing the success of the Annual Meeting as a whole.

The Society expresses its sincere thanks and profound appreciation to the firms participating in the Technical Exhibits. These are:

Abbott Laboratories, North Chicago, Illinois; Albert-Acan X-Ray Solutions, Inc., Detroit, Michigan; Ansco Products, General Aniline & Film Corporation, Binghamton, New York; Atomic Energy of Canada Limited, Ottawa, Ontario, Canada; Automatic Seriograph Corporation, College Park, Maryland; Barnes-Hind Barium Products Co., Sunnyvale, California; Bar Ray Products, Inc., Brooklyn, New York; Cascade X-Ray Specialties, Yakima, Washington; Chemtree Corporation, Harriman, New York; Controls for Radiation, Inc., Cambridge, Massachusetts; Dunlee Corporation, Bellwood, Illinois; E. I. du Pont de Nemours & Company, Inc., Wilmington, Delaware; Eastman Kodak Company, Rochester, New York; E-Z-EM Company, Inc., Great Neck, Long Island, New York; Ferrania Photo Sales Limited, Rexdale, Ontario, Canada; E. Fougera & Company, Inc., Hicksville, New York; Franklin X-Ray Corporation, Philadelphia, Pennsylvania; General Electric Company, Milwaukee, Wisconsin; The Gevaert Company of America, Inc., New York, New York; Gordon Consultants, New York, New York; The Great Ideas Program, Toronto, Ontario, Canada; Grune & Stratton, Inc., New York, New York; Halsey X-Ray Products, Inc., Brooklyn, New York; Howden Videx Products Corporation, Mount Vernon, New York; Ilford Inc., New York, New York; Keleket X-Ray Corporation, Waltham, Massachusetts; Liebel-Flarsheim Company, Cincinnati, Ohio; The Machlett Laboratories, Inc., Springdale, Connecticut; Mallinckrodt Pharmaceuticals, St. Louis, Missouri; Marcanus Distributors Incorporated, Don Mills, Ontario, Canada; Mattern Division of Dynalectron Corp., Chicago, Illinois; McAinsh & Company, Limited, Toronto, Ontario, Canada; Motorola, Communications & Electronics Inc., Chicago, Illinois; Pako Corporation, Minneapolis, Minnesota; Pennsylvania X-Ray Corporation, Glenside, Pennsylvania; Philips Electronic Equipment Ltd., Toronto, Ontario, Canada; Physicians Technical Equipment Company, Inc., New York, New York; Picker X-Ray Corporation, White Plains, New York; Pritchard X-Ray Manufacturing Ltd., Richmond Hill, Ontario, Canada; Profexray, Inc., Maywood, Illinois; W. B. Saunders Company, Philadelphia, Pennsylvania; Schick X-Ray Company, Inc., Chicago, Illinois; Frank Scholz X-Ray Corporation, Boston, Massachusetts; Siemens America Incorporated, New York, New York; E. R. Squibb & Sons, New York, New York; Smith Kline-Precision Company, Philadelphia, Pennsylvania; Standard X-Ray Company, Chicago, Illinois; Charles C Thomas, Publisher, Springfield, Illinois; United Electric X-Ray Company, Ltd., Toronto, Ontario, Canada; United States Catheter & Instrument Corporation, Glens Falls, New York; United States Radium Corporation, Morristown, New Jersey; Varian Associates, Palo Alto, California; Walker Industries, Inc., San Francisco, California; Westinghouse Electric Corporation, Pittsburgh, Pennsylvania; The Williams & Wilkins Company, Publishers, Baltimore, Maryland; Winthrop Laboratories, New York, New York; Year Book Medical Publishers, Inc., Chicago, Illinois.

NEWS ITEMS

AMERICAN ROENTGEN RAY SOCIETY ELECTS OFFICERS

At the Sixty-fourth Annual Meeting of the American Roentgen Ray Society held at the Queen Elizabeth Hotel, Montreal, Quebec, Canada, October 8 to October 11, 1963 the following officers were elected: President, Dr. Ralph M. Caulk, Washington, D. C.; President-Elect, Dr. Harold O. Peterson, Minneapolis, Minnesota; 1st Vice-President, Dr. Jarrell E. Miller, Dallas, Texas; 2nd Vice-President, Dr. D. L. McRae, Montreal, Quebec, Canada; Secretary, Dr. C. Allen Good, Rochester, Minnesota; Treasurer, Dr. Stephen W. Brown, Augusta, Georgia.

Dr. J. P. Medelman, White Bear Lake, Minnesota, was re-elected as Chairman of the Executive Council, filling the term of the deceased Dr. Everett L. Pirkey of Louisville, Kentucky.

At this meeting a new Committee, called the *Advisory Committee on Education and Research*, was created. The Chairman of this Committee is Dr. Harold G. Reineke, Cincinnati, Ohio.

The Sixty-fifth Annual Meeting of the Society will be held at the Radisson Hotel, Minneapolis, Minnesota, September 29 to October 2, 1964.

SOCIETY FOR PEDIATRIC RADIOLOGY

At the Sixth Annual Meeting of the Society for Pediatric Radiology held on October 7, 1963, in conjunction with the Sixty-fourth Annual Meeting of the American Roentgen Ray Society, at the Queen Elizabeth Hotel, Montreal, Quebec, Canada, the following officers were elected: President, Dr. R. Parker Allen, Denver, Colorado; President-Elect, Dr. Edward B. Singleton, Houston, Texas; Secretary-Treasurer, Dr. John L. Gwinn, Children's Hospital, Los Angeles 90027, California.

The Seventh Annual Meeting of the Society will be held at the Radisson Hotel, Minneapolis, Minnesota, September 28, 1964.

SYMPOSIUM ON SCINTISCANNING IN CLINICAL MEDICINE

On January 30–31, 1964, a symposium on Scintiscanning in Clinical Medicine will be held in Winston-Salem, N. C., sponsored by the Department of Radiology of the Bowman Gray School of Medicine. Subjects to be covered will include the physical, electrical and pharmacologic principles of organ scanning as well as specific discussions of brain, thyroid, parathyroid, heart, lung, liver, spleen, kidney, pancreas and bone scanning.

The Guest Faculty will include outstanding scientists from various parts of the country. Registration will be limited to 200.

For details write to J. L. Quinn, III, M.D., Nuclear Medicine, Bowman Gray School of Medicine, Winston-Salem 7, N. C.

COURSE IN MEDICAL USES OF RADIOACTIVE ISOTOPES, QUEENS GENERAL HOSPITAL

A four month course in the Medical Uses of Radioactive Isotopes will be offered by the Radiation Medicine Department at the Queens Hospital Center, Department of Hospitals, The City of New York. The course will commence on Tuesday, February 4, 1964 and will consist of weekly five hour sessions covering lectures, laboratory exercises, and clinical management of patients. Enrollment will be limited.

Apply to Dr. Philip J. Kahan, Supervising Medical Superintendent, Queens Hospital Center, 82-68 164th Street, Jamaica 32, New York.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

PRINCIPLES AND PRACTICE OF ORAL RADIOLOGIC INTERPRETATION. By H. M. Worth, F.R.C.P. (C), F.F.R., L.R.C.P. (Lond.), M.R.C.S. (Eng.), L.D.S., R.C.S. (Eng.), D.M.R.E. (Camb.), Formerly Radiologist to Guy's Hospital and Dental School; Special Lecturer in Radiology, The Faculty of Dentistry, University of Toronto; Diplomate, American Board of Radiology. Cloth. Pp. 746 with 662 illustrations. Price, $30.00. Year Book Medical Publishers, 35 E. Wacker Drive, Chicago 1, 1963.

This work is an excellent presentation of Principles and Practice of Oral Radiologic Interpretation. Throughout the entire volume, the diligent effort and attention to detail by the author and those associated with him in the compilation of the material is very apparent. The text is detailed, but easy and interesting to read. The radiographs used for the many hundreds of illustrations are magnificently reproduced.

Perusal of the table of contents with its 21 chapter headings immediately impresses one with the comprehensive character of the book. In the introduction the author discusses the principles of oral radiologic interpretation in general. The first few chapters are concerned with the normal radiographic anatomy and developmental variations and abnormalities of the teeth and jaws. The remaining chapters are devoted to essentially all of the common and rare diseases and conditions encountered in the radiographic examination of the teeth and adjacent structures.

This book can truly be regarded as a valuable addition to the library of anyone concerned with oral diagnosis. It can be utilized as a text for the student or as a reference for those engaged in practice.

HAVEN F. DOANE, D.D.S.

MALPRACTICE LAW DISSECTED FOR QUICK GRASPING. By Charles L. Cusumano, Member of the New York Bar. Cloth. Pp. 132. Medicine-Law Press, Inc., 42 Broadway, New York 4, N. Y., 1962.

It would be unwise to drive an automobile without a thorough knowledge of traffic laws. A physician would be just as unwise to attempt to practice medicine without a thorough grounding in the malpractice law. The increasing emphasis upon this subject is apparent in the host of articles now appearing in medical news media and periodicals. Most doctors have only some very vague notions about the law of malpractice, and up to now if they wanted to learn more about it they had to make a research project out of it.

This concise, easy reading text is designed to render the fundamentals of the law quickly understandable to anyone interested. It delves into pitfalls a physician should avoid, and the safeguards he should heed. It can give one a great peace of mind and self assurance, and yet make one aware of ever present danger. Its broad scope makes it valuable to dentists, nurses, and hospital administrators as well as all physicians. Radiologists are just as prone to be involved in a malpractice situation as other physicians. The hazards involved in radiation therapy as well as in the injection of various contrast materials are well known.

This book describes contractural relationships between physician and patient, duties of physicians and specialists toward patients, malpractice grounds, consent to treatment and autopsy, physician's defenses in malpractice cases, and professional insurance, these being but a few of the areas covered. An excellent bibliography is provided.

ARCH H. HALL, M.D.

CARE OF THE PATIENT IN DIAGNOSTIC RADIOGRAPHY. By D. N. and M. O. Chesney; Respectively Superintendent Teacher, School of Radiography, Coventry and Warwickshire Hospital; and Teacher-Principal, School of Radiography, The United Birmingham Hospitals. Cloth. Pp. 221, with illustrations. F. A. Davis Company, Philadelphia, Pa., 1962.

The British student radiographer must receive formal instruction in the care of the patient in the x-ray department. This excellent textbook was written to aid in that aspect of his training.

There is a comprehensive review of the many facets of patient care; in particular valuable discussions are included on the following topics: ethics; the general preparation of a patient for an x-ray examination; the handling of the unconscious, diabetic, infectious, stretcher and other special problem patients; first aid; hygiene and sterile technique; contrast media and adverse reactions; working with the mobile unit in the ward and operating room; and radiation exposure.

Further chapters outline the common special procedures performed in a radiology department and present the technologist's role in relation to the patient for each study.

The thoroughness of this text will warrant its study not only by the student, but by the veteran technologist as well.

John T. Underberg, M.D.

BOOKS RECEIVED

The Osseous System: A Handbook of Roentgen Diagnosis. Revised reprint. By Vincent W. Archer, M.D., Professor of Roentgenology, University of Virginia School of Medicine. Cloth. Pp. 331, with 441 figures. Price, $10.00. Year Book Medical Publishers, Inc., 35 East Wacker Drive, Chicago, Ill., 1963.

Dystrophia Myotonica and Related Disorders. By J. E. Caughey, M.D. (N.Z.), F.R.A.C.P., F.R.C.P. (London), Associate Professor in Neurology, Otago University Medical School, Dunedin, New Zealand; Neurologist, Dunedin Hospital; Late Visiting Scientist, National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda, Md.; Late Visiting Physician, London Post-Graduate Hospital: and N. C. Myrianthopoulos, Ph.D., National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda, Md. Cloth. Pp. 282, with many illustrations. Price, $10.00. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1963.

The Treatment of Malignant Disease by Radiotherapy. Second edition. By Ralston Paterson, C.B.E., M.C., M.D., F.R.C.S., D.M.R.E., F.F.R., lately Director of Radiotherapy, Christie Hospital and Holt Radium Institute, Manchester; Professor-Emeritus, Manchester University, England. Cloth. Pp. 556, with some illustrations. Price, $15.50. The Williams & Wilkins Company, Baltimore 2, Md., 1963.

Elementary Medical Statistics. Second edition. By Donald Mainland, M.B., Ch.B., D.Sc., F.R.S.E., F.R.S.C., F.A.S.A., Professor of Medical Statistics, New York University Medical Center. Cloth. Pp. 381, with some tables. Price, $9.00. W. B. Saunders Company, West Washington Square, Philadelphia 5, Pa., 1963.

Diseases of the Skin: for Practitioners and Students. Fifth edition. By George Clinton Andrews, M.D., F.A.C.P., Clinical Professor of Dermatology (retired), College of Physicians and Surgeons, Columbia University; Consulting Dermatologist to the Presbyterian Hospital, Columbia-Presbyterian Medical Center, New York: and Anthony N. Domonkos, M.D., F.A.C.P., Associate Clinical Professor of Dermatology, College of Physicians and Surgeons, Columbia University; Attending Dermatologist to the Presbyterian Hospital, Columbia-Presbyterian Medical Center, New York. Cloth. Pp. 749, with 605 illustrations. Price, $16.50. W. B. Saunders Company, West Washington Square, Philadelphia, Pa., 1963.

The Treatment of Radiation Injury. Publication 1134. Paper. Pp. 19. Price, $1.00. The National Academy of Sciences, National Research Council, 2101 Constitution Avenue, Washington, D. C., 1963.

ABSTRACTS OF RADIOLOGICAL LITERATURE

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Neck and Chest

Steiner, R. E. *et al.*: Mitral regurgitation..... 1329
Kane, J. J. *et al.*: Size of the left atrium by x-ray examination in the differentiation of interatrial and interventricular septal defects in congenital heart disease................ 1329
Cayler, G. G. *et al.*: Pericarditis with effusion in infants and children................... 1330
Straube, K. R. *et al.*: Death following selective right ventricular angiocardiography; a case report............................ 1330
Lister, J.: An unusual variation of oesophageal atresia.......................... 1331

Abdomen

Bourdet, P., Delahaye, R. P., and Allain, Y.: Refinements of technique for the radiologic diagnosis of post-traumatic diaphragmatic hernias and eventrations........... 1331
Marks, I. N. *et al.*: The natural history of corrosive gastritis: report of five cases...... 1332
Caldwell, W. L., and Floch, M. H.: Evaluation of the small bowel barium motor meal; with emphasis on the effect of volume of barium suspension ingested............ 1332
Salzman, E., and McClintock, J. T.: Opacification of the small bowel with intravenously administered contrast medium............ 1332
Lundberg, G. D., and Linder, W. R.: Whipple's disease with associated splenomegaly and pancytopenia....................... 1333
Corry, D. C.: Milk in diverticula of colon... 1333
Poutasse, J. D.: Unusual colon manifestations of lymphosarcoma: report of 2 cases........ 1333
Miller, R. E., and Rhamy, R. K.: Acute perforation in infants....................... 1334
McAlister, W. H. *et al.*: Lethal effects of tannic acid in the barium enema; report of three fatalities and experimental studies.... 1335
Walker, L. A., and Weens, H. S.: Radiological observations on the lesser peritoneal sac.................................... 1335
Samuel, E. *et al.*: Radiology of the post-operative abdomen.......................... 1335
Jaedke, W., and Behrens, D.: Calcified metastases in the liver from a primary gastric carcinoma: with a discussion of the question of calcium deposition in mucin producing carcinomata.............................. 1336
Grunfeld, G. O. *et al.*: Radiologic aspects of thallium poisoning...................... 1336

ROENTGEN DIAGNOSIS

Neck and Chest

Steiner, R. E., Jacobson, G., Dinsmore, R., and Parizel, G. Mitral regurgitation. *Clin. Radiol.*, April, 1963, *14*, 113–125. (From: Departments of Radiodiagnosis and Medicine, Hammersmith Hospital and Postgraduate Medical School of London, London, W. 12, England.)

The assessment of mitral regurgitation is uncertain by clinical and roentgenologic criteria, particularly if there is also mitral stenosis present. For this reason an attempt was made to evaluate the method of left ventricular angiocardiography as a means of estimating mitral regurgitation. In patients with mitral stenosis without mitral regurgitation, contrast material injected into the left ventricle will not regurgitate into the left atrium. The study has been limited to 32 adults. These were divided into two groups: one of 20 with mitral regurgitation and a second group of 12 patients without mitral regurgitation. The division was made purely on roentgenologic grounds.

Left ventricular angiocardiography by the percutaneous route from the femoral artery using a Kifi catheter is preferable to arteriotomy. Film sequences at 6 films per second provide adequate and satisfactory anatomic information about the left atrium and ventricle during various phases of the cardiac cycle. The only direct and objective sign of mitral regurgitation is the appearance of contrast medium in the left atrium following a left ventricular injection. The first difficulty encountered in this assessment is rhythm changes, particularly ectopic cardiac beats during the injection phase. The second difficulty in assessing the amount of regurgitated contrast medium is due to the dilution effect of contrast material in the atrium, and this is largely dependent on atrial size. The third consideration is the stroke volume of the left ventricle and the effectiveness of its systolic contraction. These two factors will inevitably affect the onset of contrast regurgitation and the time of maximal opacification of the left atrium. It is the authors' impression that an estimate of regurgitated contrast material into the atrium expressed in atrial density is a most important sign in assessing mitral regurgitation.

There is a loose correlation between left atrial size and mitral incompetence but there is no satisfactory correlation between left ventricular size and mitral incompetence. Timing of left atrial opacification, initial appearance of contrast medium and maximal opacification time seem to be of no value in assessing the degree of mitral incompetence. The regurgitant jet of contrast medium past an incompetent mitral valve can occasionally be seen on the early lateral films in the angiocardiographic series, but it is probably better demonstrated by cineangiography. Paradoxical pulsation of the left atrium as a sign of mitral incompetence is not specific. *There is only one sign of importance in assessing mitral regurgitation: the appearance of contrast medium in the left atrium and the somewhat objective assessment of the degree of left atrial opacification*—always bearing in mind left atrial size.—*Samuel G. Henderson, M.D.*

Kane, John J., Pettit, Harold S., Pappas, Anthony, and Boone, John A. Size of the left atrium by x-ray examination in the differentiation of interatrial and interventricular septal defects in congenital heart disease. *South. M. J.*, May, 1963, *56*, 458–460. (From: Departments of Medicine and Radiology, Medical College of South Carolina, Charleston, S. C.)

With the advent of surgical procedures to correct congenital cardiac defects, precise anatomic diagnosis has become of great importance. Determination of the size of the left atrium by roentgenologic examination plus clinical and electrocardiographic findings proved to be a very reliable method of differentiating between interatrial and interventricular septal defects. With either, a left to right shunt increases the pulmonary blood volume. In the case of the ventricular defect, the left atrium enlarges. With interatrial septal defects, the defect itself affords a route to decompress the left atrium and hence it does not enlarge.

Some exceptions were noted. Left atrial enlargement was evident in 3 out of 50 cases of interatrial septal defects but in these congestive heart failure was present at the time of the study. In 30 cases of interventricular septal defects, 3 showed a normal sized left atrium but in 2 there also were interatrial defects and 1 had mild pulmonary stenosis with normal vascularity of the lung fields as found by roentgen study.

The authors' experience showed operation or autopsy to be more reliable in the final diagnosis than cardiac catheterization and angiocardiography. Absence of posterior displacement of the barium-filled esophagus is not reliable evidence of left atrial enlargement. Conversely, posterior displacement of the esophagus may occur on the basis of gross enlargement of the right ventricle which displaces the entire heart posteriorly. Based upon 50 cases of interatrial septal defects and 30 cases of interventricular septal defects, the authors concluded that in the presence of enough left to right shunt to increase vascularity of the lung fields, the left atrium will be enlarged in interventricular septal defects and not in interatrial septal defects.—*John H. Harris, M.D.*

CAYLER, G. G., TAYBI, H., RILEY, H. D., JR., and SIMON, J. L. Pericarditis with effusion in infants and children. *J. Pediat.*, Aug., 1963, *63*, 264–272. (From: Departments of Pediatrics and Radiology, Children's Memorial Hospital, University of Oklahoma Medical Center, Oklahoma City, Okla.)

The authors review the case histories of 17 infants and children in whom the diagnosis of pericarditis with effusion was made over a 3½ year period. The post-pericardiotomy syndrome accounted for 5 of the cases, rheumatic fever for 4 and pyogenic infection for 3.

The diagnosis of pericarditis with effusion is difficult as a pericardial friction rub occurs in approximately 50 per cent of the cases. The authors feel that the following clinical findings usually indicate the presence of a pericardial effusion:

1. marked cardiac enlargement without associated pulmonary congestion
2. pulsus paradoxus
3. obliteration of the retrosternal space without electrocardiographic evidence of right ventricular enlargement
4. sudden development of cardiac enlargement associated with a pyogenic long bone or renal infection

The incidence of error is sufficiently great that further procedures are often necessary. Pericardiocentesis is difficult and dangerous. A roentgenogram with a radiopaque catheter against the lateral margin of the right atrial wall is a simple and safe technique. This can rule out the presence of an effusion when the distance between the tip and the right heart border is not increased. However, a false negative examination may be obtained when the tip is not against the lateral cardiac margin. Cardiac and pulmonary vascular pulsation did not prove reliable. The kymographic technique is not applicable to infants and children because of the lack of cooperation. Serial venous angiocardiography has proved the most reliable method for the demonstration of pericardial fluid. It is, however, a fairly tedious procedure and carries a small, but definite risk. Two cases of localized effusion in association with a pericardial diverticulum were missed using this technique.—*Barry Gerald, M.D.*

STRAUBE, KURT, R., DOTTER, CHARLES T., and O'DELL, JAMES. Death following selective right ventricular angiocardiography; a case report. *Radiology*, April, 1963, *80*, 616–621. (Address: 3181 S. W. Sam Jackson Park Road, Portland 1, Ore.)

Various forms of mechanical intrathoracic injury associated with cardiac catheterization have been reported including endocardial laceration, perforation of the heart, intramyocardial and intrapericardial extravasation of injected fluids, hemopericardium, hemothorax, pneumothorax, catheter amputation, and catheter knotting around chordae tendineae, requiring open heart surgical release. The authors present a case report of an additional type of injury, fatal to their patient, consisting of an endocardial and apical laceration with a large hematoma of the intraventricular septum.

The patient, a 6 year old white female with tetralogy of Fallot, was subjected to selective right ventricular angiocardiography to determine the feasibility of total operative correction. A left sided Blalock anastomosis had been done at the age of 10 months. Under general anesthesia, a spring-guided polyethylene catheter was manipulated into the right ventricle and the guide was removed, after which both right ventricular pressure and the electrocardiogram were continuously monitored. There were ectopic ventricular beats associated with the passage of the catheter and the first of two injections. The first injection consisted of 20 cc. of sodium methalamate, 80 per cent, with filming done in the frontal plane. The series of frontal films showed a minor extravasation of contrast medium into the right ventricular wall. Damping of the pressure curve was noted between the first and second injections and the catheter was withdrawn until undamped pressure waves were again obtained. A second injection with the same volume of medium was performed in the lateral projection which produced massive extravasation into the septal myocardium and the catheter was immediately removed. During the secoud injection ectopic ventricular beats appeared with a variable QRS configuration but following the injection the electrocardiogram returned to its previous form except for slight depression of the initial portion of the T-wave. A chest roentgenogram made 15 minutes after the second injection demonstrated little remaining opacity. The patient was returned to the ward where she was placed in an oxygen tent because of cyanosis and rapid respiration. The systolic blood pressure remained at approximately 80 mm. Hg for about 4 hours after which the pressure gradually declined, cyanosis deepened, and the patient expired approximately 10 hours after the time of injury.

Autopsy revealed a tetralogy of Fallot with a right sided aortic arch and descending aorta. The heart weighed 200 grams and presented a subepicardial band of blood along the vessel sheaths of the anterior and posterior descending coronary arteries. When the heart was opened, the ventricular septum was found to be unusually thick, approximately 5.5 cm., and was superficially torn in an area about 1 cm. in diameter at the right ventricular apex. The ventricular septum was sectioned serially to reveal a 5 cm. spherical hematoma which was continuous with the septal laceration and the apical epicardial tissue. The dissection had proceeded from the torn area upward into the body of the septum and then downward through the apical myocardium. The pertinent features of this case are summarized to support the belief that death was due to the hematoma rather than to a toxic effect of the contrast agent.

The authors emphasize that if there is a single useful purpose in their report, it is related to the existence and meaning of warning signs which they believe should prevent further similar complications. These consisted of minor myocardial infiltration occurring with the first injection and the subsequent appearance of damping of the right ventricular pressure curve despite an evidently patent catheter lumen. The point is stressed that the presence of catheter side holes completely destroys the value of an undamped pressure curve as an indicator of intravascular tip location, just as it amplifies the significance of pressure damping in a clot-free catheter. These infiltrations can probably occur with all types of catheters but are less likely with a closed-end instrument. Even though contrast medium may not be visualized in the myocardium, a reliable sign of myocardial infiltration by contrast agent is the immediate demonstration of opacified coronary veins.

The authors conclude that in the event of unexplained pressure damping and minor myocardial infiltration, further evidence of the desired position of the catheter tip should be obtained through trial injection of contrast agent during fluoroscopy. Lacking this, no further injection should be attempted.—*Edward B. Best, M.D.*

Lister, James. An unusual variation of oesophageal atresia. *Arch. Dis. Childhood*, April, 1963, *38*, 176–179. (From: Nuffield Department of Paediatric Surgery, Institute of Child Health, University of London, and the Queen Elizabeth Hospital for Children, London, England.)

Approximately 90 per cent of all cases of esophageal atresia are found to have a blind upper pouch and a fistula between the lower pouch and the trachea. The common association of other congenital anomalies such as duodenal atresia, imperforate anus and congenital heart disease suggests a generalized insult to the developing embryo. Another 8 per cent of the cases have esophageal atresia with no fistula, while the remaining cases are composed of varying less common anomalies. Two cases with simple septal obstruction and tracheo-esophageal fistula, connecting the trachea to the esophagus distal to the site of obstruction, are described. A common denominator of both cases was the low level of the blind upper pouch, reaching below the fifth dorsal vertebra. This may be a diagnostic clue to this particular form of fistula.

Theories regarding the etiology of this condition are discussed. It has been shown that intestinal atresia in the form of an occluding diaphragm may be produced by local interference with blood supply. The author suggests a similar etiology for tracheoesophageal fistula, possibly due to extrinsic pressure from an arteria aberrans, the remnant of the fourth right aortic arch.—*David Corbett, M.D.*

ABDOMEN

Bourdet, P., Delahaye, R. P., and Allain, Y. Artifices de technique dans le diagnostic radiologique des hernies et des eventrations diaphragmatiques post-traumatiques. (Refinements of technique for the radiologic diagnosis of post-traumatic diaphragmatic hernias and eventrations.) *J. de radiol., d'électrol. et de méd. nucléaire*, March–April, 1963, *44*, 167–178. (From: Service de Chirurgie thoracique et Services d'Electroradiologie de l'H. M. I. Percy [Clamart], et de l'H. M. I. Dominique-Larrey [Versailles], France.)

The diagnosis of eventration of the diaphragm as well as of hernias through the diaphragm can be made with certainty by means of roentgenologic examinations. The authors limit their discussion to hernias and eventration occurring as a result of closed injuries (thoraco-abdominal and thoracolumbar). They define hernia as the engagement of an abdominal viscus in a natural parietal orifice, through a rupture in the continuity of the diaphragm. The definition of eventration is less concise and less clear. It is the result of an elevation, drawing away, relaxation or disturbance of innervation of the diaphragm. In diaphragmatic herniation the abdominal organs may be in contact with the thoracic organs while in eventration, because of the elevation of the diaphragm, the abdominal organs are within the thorax, yet not in continuity with the thoracic organs.

Roentgenologic examinations may be performed (1) by roentgenoscopy for the determination of the diaphragmatic excursion, which may be limited, absent, or at times paradoxical; and (2) by roentgenography in an attempt to try to determine the continuity of the diaphragm, as well as its position and status.

On a plain roentgenogram it may be possible to identify a triangle which is bordered superiorly by the diaphragm, medially and below by the lateral wall of the stomach, and laterally and below by the medial wall of the colon.

Further roentgenologic examinations may be carried out by means of contrast studies. By introducing effervescent substances, liberating a gas which may augment the gas bubble of the stomach, the diaphragm may be better delineated. By means of a pneumoperitoneum the continuity of the diaphragm is delineated in eventration; the presence of a rupture or hernia through the diaphragm will result in a pneumothorax. Pleural adhesions, effusion and other causes of pleural density will interfere with the usefulness of this procedure.

A more accurate roentgenologic study would be to opacify the stomach with orally administered barium and the colon with a barium enema. The relative position of these organs in relation to each other as well as to the chest organs can best be brought out with the patient in the Trendelenburg position.

Studies of the right diaphragm may be carried out in a similiar manner. In eventration of the right diaphragm, air from a pneumoperitoneum gives a crescent shaped area of decreased density under the diaphragm, whereas a pneumothorax will result if there is a rupture or hiatus in the diaphragm. Furthermore, the liver and gallbladder may participate in a herniation through the diaphragm; usually a part of the liver may be herniated. The position of the gallbladder may be elevated and is best demonstrated when opacified. The ducts appear "taut."

Four case reports and 16 sketches and illustrations accompany this interesting article.—*William H. Shehadi, M.D.*

Marks, I. N., Bank, S., Werbeloff, L., Farman, J., and Louw, J. H. The natural history of corrosive gastritis: report of five cases. *Am. J. Digest. Dis.*, June, 1963, *8*, 509–524. (From: Department of Medicine, Wernher and Beit Medical Laboratories, University of Cape Town Observatory, Cape Town, South Africa.)

Five cases in which corrosive substances were ingested are reported in detail. Esophageal involvement was a prominent feature in the patient who had swallowed potassium hydroxide and in 1 of the 4 patients who had taken hydrochloric acid. The roentgenologic features of the stomach were remarkably similar in 4 of the 5 patients; diffuse narrowing and rigidity of the distal half of the stomach, maximal in the pyloric region, was the rule by the end of the second or third week, and 3 of the 4 also had evidence of ulceration of the lesser curvature in the region of the angulus. Repeat barium studies in 2 of these 4 patients revealed that the lesion had progressed to virtually complete pyloric stenosis at the end of 11 weeks. In the fifth patient the stomach emptied normally on the nineteenth day, but appeared small, scarred, and contracted and its lumen was almost completely occluded at the end of the fourth month. Dilatation of the second and third parts of the duodenum was present in 3 of the 5 patients, and a fluid level was noted in the dilated portion of the duodenum in 2 of them.

Clinically, severe pain and hematemesis were the outstanding symptoms; the clinical findings were hematemesis, severe epigastric pain and retching and vomiting of blood stained gastric contents. The changes in the stomach, roentgenographically, simulated carcinomatous infiltration of the antrum. This is especially true in those patients in which a of corrosive ingestion is lacking. This erroneo nosis may also be made on clinical groun weight loss is prominent, and achlorhydria or hypochlorhydria is the rule; indeed the gastr may appear cartilaginous and resemble neopl filtration at laparotomy. Three of the patie suicidal, while in 2 the corrosive substance w inadvertently. Surgery was carried out on al with gastrectomy being done on 3.

Attention is also drawn to the finding of lo albumin values in patients with corrosive gas is tentatively suggested that the latter m stitute another cause of protein-losing gast The clinical, roentgenologic and pathologic and the surgical aspect are considered in detai cases reported.—*C. Peter Truog, M.D.*

Caldwell, William L., and Floch, H. Evaluation of the small bowel motor meal; with emphasis on the e volume of barium suspension i *Radiology*, March, 1963, *80*, 383–39 dress: Rodriguez U. S. Army Hospit 851, New York, N. Y.)

Many methods of examination of the sm have been devised, some of them very com

The authors compared 2 methods in 32 pa one method using 8 ounces of barium mixtur the other 16 ounces of the same mixture. The interval between the examinations was 5 d tients receiving no treatment in the meanti half of the patients had tropical sprue. Th time for 8 ounces averaged 3 hours 15 min was significantly less with 16 ounces, ave hours 15 minutes. Also, the roentgenograms 16 ounce examination were more satisfactor terpretation exhibited better visualizatio loops of the small intestine, and showed less tion.

The conclusion is reached that the 16 ou glass) method is more satisfactory for good di small bowel examination, and should be pre the 8 ounce (one glass) method.—*James C M.D.*

Salzman, Emanuel, and McClintock T. Opacification of the small bowel travenously administered contrast *Radiology*, May, 1963, *80*, 748–752. (Denver General Hospital, Denver 4,

Opacification of the small bowel in the cat observed following the intravenous administ high doses of sodium diatrizoate (1 to 3 gm., addition to the anticipated visualization of bladder and urinary tracts, serial roentge have shown accumulation of the contrast within the lumen of the small bowel about utes after the injection with, also, faint opacification of the bowel wall.

To prove that the opacification of the small bowel is due to contrast medium excreted by the bowel wall, the authors ligated the bowel wall at three sites: (a) the duodenum distal to the papilla of Vater, to exclude excretion of the contrast medium from the biliary tract and pancreas; (b) the mid small bowel; and (c) the terminal ileum. Serial roentgenograms made after injection of sodium diatrizoate showed opacification of the small bowel, as well as the gallbladder and urinary tract, but no visualization of the colon. When the terminal ileum was patent, the colon was opacified by contrast medium transported by peristalsis from the small bowel. The opacification of the colon was not the result of excretion of the medium by the colon wall.

In addition, the authors noted an enhancement of visualization of the small bowel in nephrectomized cats, probably due to a prolonged elevation of the blood level of contrast medium.

As sodium diatrizoate is not significantly absorbed from the lumen of the bowel in cats after oral administration, it appears likely that the intravenously injected contrast medium is excreted by the small bowel mucosa by a mechanism of active transport rather than simple passive diffusion.

Clinically, the authors feel that it is important to recognize that opacification of the small bowel may occur following intravenous urography in patients with renal insufficiency or after high dose angiography. This may prove to be helpful in explaining unusual or unexpected densities on abdominal roentgenograms.

It is conceivable that additional advances in knowledge of the excretion mechanism of the bowel may ultimately lead to an intravenous test for visualization of the small bowel.—*Ralph Bowman, M.D.*

LUNDBERG, GEORGE D., and LINDER, WILLIAM R. Whipple's disease with associated splenomegaly and pancytopenia. *A.M.A. Arch. Int. Med.*, Aug., 1963, *112*, 207–211. (From: Pathology Service and the Department of Medicine, Brooke General Hospital, Brooke Army Medical Center, Fort Sam Houston, Tex.)

The authors report a case of Whipple's disease complicated by splenomegaly and pancytopenia which to their knowledge is the first such association described.

The patient, a 69 year old white male, had the diagnostic interstitial infiltrate of periodic acid-Schiff (PAS)-positive macrophages in the lamina propria characteristic of Whipple's disease, as well as polyserositis, diarrhea, steatorrhea, weakness, weight loss, hypotension, and cutaneous pigmentation. In addition, he showed peripheral blood pancytopenia, splenomegaly and a normal bone marrow, allowing consideration of hypersplenism. He improved for a time on a glutin-free diet, vitamins, calcium lactate and steriods, but finally developed an overwhelming infection and died.

For several years there have been two opposing theories of hypersplenism. Doan proposed that excessive phagocytosis of formed elements of the blood by an enlarged hyperplastic spleen is the mechanism of splenic hyperfunction. Dameshek has suggested that the spleen may exert an excessive inhibitory action upon the bone marrow in these cases.

An attractive new theory is that hypersplenism is an expression of an autoimmune response; the frequent improvement in the hypersplenic state following steroid administration, as in this case, would support this theory.—*Francis P. Shea, M.D.*

CORRY, D. C. Milk in diverticula of colon. *Brit. M. J.*, April 6, 1963, *1*, 929–930. (Address: Surgeon, United Oxford Hospitals, England.)

Twelve patients in a series of 120 cases of diverticulitis were referred to the author because of abdominal pain and frequent loose stools often containing mucus and blood. The symptoms were frequently suggestive of carcinoma of the left colon. Each patient had been on a diet containing considerable milk and cream. In each case the symptoms were relieved by reducing or eliminating these dairy products from the diet.—*David Corbett, M.D.*

POUTASSE, J. DAVID. Unusual colon manifestations of lymphosarcoma: report of 2 cases. *Am. J. Digest. Dis.*, June, 1963, *8*, 545–556. (From: Department of Radiology, University of California Medical Center, San Francisco 22, Calif.)

The author reports 2 cases of lymphosarcoma of the large bowel. Case 1 was a 58 year old white woman who was seen on February 23, 1961 for investigation of edema, hypoproteinemia and bowel disease. The patient was first seen in the outpatient department of the hospital in 1957 at which time sigmoidoscopy revealed a diffuse pseudopolyposis or cobblestone appearance of the rectum and sigmoid. Barium enema examination gave evidence of finely serrated distensible colon without a localized colonic mass. The terminal ileum showed mucosal irregularity and destruction. The appearance of the colon was thought to be compatible with a diagnosis of ulcerative colitis. A rectal biopsy was interpreted as lymphoid hyperplasia.

In November of 1957, the patient was again seen in the outpatient department and at this time a diagnosis of a lymphosarcoma of the nasopharynx was made; she received radiation therapy to this lesion. Check-up studies at frequent intervals thereafter revealed no recurrence of localized disease in the treated area. She was also free of gastrointestinal symptoms except for occasional bouts of diarrhea.

Barium enema examination in 1958 again showed a finely serrated outline of the colon with occasional small polypoid filling defects. At this time she had a generalized edema which was thought to be on the basis of hypoproteinemia.

Sigmoidoscopy in 1960 showed no change from the previous examination, but barium enema study revealed in addition to the former findings a large intraluminal mass in the cecum. Small bowel and rectal biopsies were interpreted as being consistent with a lymphosarcoma.

The patient was treated with chlorambucil, 10 mg. daily, from June 1, 1961 to June 20, 1961. At this time the medication was discontinued because the white blood cell count dropped below 3,000. The patient has been completely free of symptoms since then with disappearance of the abnormal roentgenographic findings in the colon. In commenting on this patient, the author feels that the significance of the abnormal roentgenographic findings was overlooked; these consisted of a serrated colonic outline, rare small polypoid colonic defects, absence of colonic irritability and thickened haustral folds.

Case II was also a 58 year old woman. She was well until June, 1958 at which time she had symptoms of a small bowel obstruction and she underwent exploratory laparotomy at another hospital. A fairly large, soft tumor in the ileocecal region was found and a right colectomy was performed. Numerous large lymph nodes were present in the mesentery of the right colon and small bowel. A radical resection of this portion of the bowel was then performed with an ileotransverse colostomy. The pathologic diagnosis was that of a lymphocytic lymphosarcoma. The patient was well until 1959 when she saw her physician because of cervical, axillary and inguinal lymphadenopathy. A biopsy of the right cervical lymph node showed lymphosarcoma. She was treated with chemotherapeutic agents, resulting in regression of the lymphadenopathy.

In August, 1960, she returned to her physician with moderately enlarged submaxillary lymph nodes. While undergoing local radiation therapy she experienced marked abdominal cramps and diarrhea. A barium enema study revealed the entire colon to be diffusely filled with small, round, marginated polypoid defects of uniform size. The defects measured approximately 0.5 cm. Some of the haustral folds appeared thickened. After an unsuccessful course of chemotherapy, she was treated with external radiation. Following delivery of 1,000 r midplane calculated dose to the entire abdomen, a second barium enema study was done. The roentgenogram revealed that the previous polypoid lesions had almost totally regressed. Clinically the patient was asymptomatic. The author's comment on this case is that it demonstrated the honeycomb and cobblestone appearance of the colon due to lymphosarcoma.

In the discussion the author states that lymphosarcoma is a malignant primary neoplasm of lymphoid origin of unknown etiology. It may manifest itself as a single focus but, far more frequently, as multicentric foci. It may afflict patients of any age but more commonly those in the fifth decade, and women more often than men. In differential diagnosis ulcerative colitis must be considered. Larger polypoid defects of the colon may simulate the familial polyposis or the Peutz-Jeghers syndrome. The normal mucous glands of the colon when filled with barium may simulate the honeycomb appearance of a lymphosarcoma.

The conclusion is reached that roentgenographically the disease process may simulate familial polyposis, ulcerative colitis or mucous glands of the colon. Roentgenologic differentiation from ulcerative colitis may be particularly difficult. Absence of spasm and irritability of colon may be noted during the examination in the presence of lymphosarcoma.—*C. Peter Truog, M.D.*

MILLER, ROSCOE E., and RHAMY, ROBERT K. Acute perforation in infants. *Surg., Gynec. & Obst.* July, 1963, *117*, 61–66. (From: Departments of Radiology and Urology, Indiana University School of Medicine, Indianapolis, Ind.)

Spontaneous rupture of the intestinal tract during the first few hours or days of life has a very grave prognosis unless treated surgically. The perforation usually involves the stomach, but occasionally it may involve the duodenum or colon as well.

Stomach perforation is more common in boys and is often associated with prematurity or various congenital defects. In approximately one-half of the cases the perforation is caused by a congenital defect in the musculature of the stomach.

Almost uniformly, perforation of the duodenum has been caused by peptic ulceration. Approximately 40 per cent of the ulcers in children are associated with bleeding.

Perforation of the colon can occur anywhere in the colon but in half of the cases reported the transverse colon was involved. The etiology is frequently associated with muscular defects or *Pseudomonas aeruginosa.*

Clinically the child is well for the first few days of life and then suddenly develops marked abdominal distention, shock, and commonly with duodenal perforation hematemesis.

Roentgenographically, abdominal distention and a large pneumoperitoneum exist in all of these patients. A pathognomonic roentgen sign consisting of an oval air shadow outlining the peritoneal cavity and resembling a football or air dome is described. The shadow is divided in its cephalad portion along the central longitudinal axis by a narrow streak due to the falciform ligament. Occasionally it is also divided in its caudal half by a similar streak representing the urachus.

SUBJECT INDEX TO VOLUME 90

(ab) = abstract (E) = editorial

A. Stanley Kirkland, 1890–1963 (E), 1309
Abdomen, post-operative, radiology of (ab), 1335
Adenoma of duodenal bulb; case report, 753
Adolescence, painful heel in (ab), 1111
Adrenal glands, angiographic demonstration of (ab), 215
  hemorrhage, acute massive, of newborn, the radiologic features of (ab), 216
Afterloading in interstitial and intracavitary radiation therapy, 386
Albright's syndrome in adult male: report of atypical case with psychiatric symptoms (ab), 1114
American Roentgen Ray Society, Harry W. Dachtler—last Charter Member of (E), 1310
  Instruction Courses of Sixty-fourth Annual Meeting of (E), 411
  Sixty-fourth Annual Meeting of (E), 199, 1302
  Sixty-fourth Annual Meeting, preliminary program, 201
Aneurysm, isolated arteriosclerotic, of common iliac artery; report of 3 cases, 166
  of azygos vein, etiology undetermined, 575
  of hepatic artery; importance of angiographic visualization, 578
Angiocardiography, selective right ventricular, death following; case report (ab), 1330
Angio-conray, sodium iothalamate, in selective angiography; further evidence of low toxicity, 1287
Angiogram, cerebral, in agenesis of corpus callosum, 522
  cerebral, normal, effect of changes of end expiratory carbon dioxide tension on, 506
Angiographic demonstration of the adrenal glands (ab), 215
  differential diagnosis between vascularized malignant glioma and intracranial arteriovenous malformation, 512
  features of convexity subdural hematomas with emphasis on differential diagnosis between unilateral and bilateral hematomas, 445
Angiography and normal anatomy of drainage system, insula and deep middle cerebral venous, 472
  further evidence of low toxicity, sodium iothalamate, angio-conray, in selective, 1287
  in patients with cerebrovascular disease, clinical evaluation of conray for, 1281
  of systemic pulmonary circulation, 614
  percutaneous left brachial, renal (ab), 214
  renal, by retrograde femoral catheterization as aid to diagnosis of renal tumors (ab), 1105
  serial, cerebral circulation time in cerebral vascular disease, measured by, 490
  vertebral basilar and carotid, by injection of brachial artery; cannula (non-catheter) technique, 546
Annular pancreas in infancy; report of 3 cases, 740
Aortography, percutaneous left brachial, 564
  percutaneous transfemoral, in gynecology and obstetrics (ab), 212
Aplasia of pulmonary artery (ab), 1101
  of trochlea—an original mutation (ab), 1109
Apprehension, effects of, on radiorenogram, 141
Arteriography, percutaneous transfemoral selective of brachiocephalic vessels, 554
  renal, selective, 124
  retrograde, in diagnosis of bladder tumors (ab), 1105
Arteriosclerotic aneurysm, isolated, of common iliac artery; report of 3 cases, 166
Arteriovenous malformation, intracranial, angiographic differential diagnosis between vascularized malignant glioma and, 512
Atrium, left, size of, by x-ray examination in differentiation of interatrial and interventricular septal defects in congenital heart disease (ab), 1329
Autoradiographic and alizarin techniques in study of bone growth, comparison of (ab), 1118
Autosomal chromosome abnormalities, relationship between congenital anomalies and (ab), 442
Autotomography and pneumoencephalography, improved chair for, 184
Azygos vein, etiology undetermined, aneurysm of, 575

Barium enema, lethal effects of tannic acid in; report of three fatalities and experimental studies (ab), 1335
  suspension ingested, evaluation of small bowel barium motor meal; with emphasis on effect of volume of (ab), 1332
Basilar impression; contribution to neuroradiologic diagnosis and clinical symptomatology (ab), 1101
Biliary fistulae, spontaneous internal, clinical and radiological features of (ab), 890
  tract, internal fistulae, 835
Billroth-I recurrent ulcer (ab), 888
Biochemical basis of reproductive death in irradiated cells, 907
Bladder cancer, experience with preoperative irradiation followed by radical cystectomy for treatment of, 1016
  distention (voluntary), effect of, on intravenous pyelogram; experimental study, 37
  neck dysfunction, genitourinary tract function, cineflourographic investigation of, 1

  - tumors, retrograde arteriography in diagnosis of (ab), 1105
  - tumors with conventional and megavoltage radiation therapy, survival rate after treatment of (ab), 668
- BONE, malignant, pain relief with radioiodine (ab), 671
  - metastases, use of strontium-85 in evaluation of, preliminary report (ab), 671
- BOOK REVIEWS
  - Clinical Radiology of the Biliary Tract. By William H. Shehadi. With a chapter on Radiation Therapy by Harold W. Jacox, 207
  - An Atlas of Detailed Normal Pneumoencephalographic Anatomy. By Giovanni Di Chiro, 207
  - Isodose Charts and Depth Dose Tables for Medium Energy X Rays. Prepared by K. C. Tsien and M. Cohen, 432
  - Radioisotopes in Cardiovascular Disease. Edited by Charles K. Friedberg, and (Guest Editor) Solomon Silver, 662
  - Unit-Step Radiography; Simplification of Medical Radiography through Manual and Automatic Use of an Exposure Value Scale (XVS) System and Standardization. By Gerhart S. Schwarz, 882
  - The Year Book of Radiology (1962–1963 Series). Edited by J. F. Holt, H. W. Jacox, and M. M. Kligerman, 1092
  - Tumors of the Eye. By Algernon B. Reese, 1092
  - Principles and Practice of Oral Radiologic Interpretation. By H. M. Worth, 1326
  - Malpractice Law Dissected by Quick Grasping. By Charles L. Cusumano, 1326
  - Care of the Patient in Diagnostic Radiography. By D. N. and M. O. Chesney, 1326
- BOWEL preparation for radiologic examination: comparison of techniques (ab), 888
- BRAILSFORD, linear thoracic paraspinal shadow of, displacement of; early sign in osteomyelitis of thoracic spine, 1231
- BRAIN, circumscribed gas-gangrene abscess of: case report together with account of literature (ab), 665
  - tuberculoma of, 1185
- BREAST, soft tissue roentgenography of; analysis of factors which influence roentgenographic quality and description of new technique, 359
- BREMSSTRAHLUNG radiation with scintiscanner, determination of distribution of P^{32} in phantoms and in patients by detection of, 325
- BRIM SIGN; new sign found in Paget's disease (osteitis deformans) of pelvis, 1267
- BRONCHIAL CARCINOMA, high-dose mustine therapy for (ab), 670
  - revealed by barium-filled esophagus, retrotracheal lymphadenopathy in, 792
- BRONCHOGRAPHIC CRYSTALLINE-INCLUSION PNEUMONIA due to hytrast (ab), 1101
- BUCKY, GUSTAV P., M.D., 1899–1963 (E), 661

- CO_2-INSUFFLATION, soft tissue diagnosis with (ab), 443
- CALCANEUS to navicular, hereditary transmission of congenital coalition of (ab), 1110
- CANCER, esophageal, diagnostic problems of; relationship to achalasia and hiatus hernia, 778
  - of gastric cardia associated with esophageal hiatus hernia (ab), 888
  - of laryngopharynx, advanced, combined therapy irradiation and surgery for, 1023
  - of urinary bladder, advanced, supervoltage radiation therapy in (ab), 1115
- CARBON DIOXIDE tension on normal cerebral angiogram, effect of changes of end expiratory, 506
- CARCINOMA, bronchial, high-dose mustine therapy for (ab), 670
  - endometrial, 1011
  - of cervix, isotope renogram; preliminary report, 149
  - pelvic, contribution of cavography to detection of lymph node metastases of (ab), 441
  - squamous cell, of the head and neck, combined irradiation and chemotherapy in treatment of, 246
- CATHETER, single lumen balloon, for percutaneous insertion: approach to occlusion angiography, 650
- CAUDA EQUINA, lumbar spondylosis with compression of (ab), 440
- CAVERNOSOGRAPHY, application of, in diagnosis of lesions of penis, 169
- CAVOGRAPHY, contribution of, to detection of lymph node metastases of pelvic carcinoma (ab), 441
- CELIOGRAPHY with iothalamic acid; experimental studies in dogs and rats, 723
- CEREBRAL cavities following ventricular punctures in infants (ab), 1101
  - circulation time in cerebral vascular disease measured by serial angiography, 490
  - pneumography, ventricular span in, 1176
- CEREBROVASCULAR DISEASE, clinical evaluation of conray for angiography in patients with, 1281
- CERVICAL diskography; help or hindrance in evaluating neck, shoulder, arm pain?, 1208
  - lymph node involvement in oral cancer, 978
  - lymph node metastases from carcinoma of hypopharynx, treatment of, 997
  - lymph nodes, metastases in, from oropharyngeal carcinoma; treatment and results, 990
  - metastases from laryngeal cancer, end results of treatment of, 1004
  - spondylotic myelopathy (ab), 1109

  vertebra, first, between ages six to seventeen, incidence of ponticulus posticus of (ab), 667
Cervix, carcinoma of, isotope renogram in; preliminary report, 149
Chair, improved, for pneumoencephalography and autotomography, 184
Chemotherapy and irradiation, combined, in treatment of squamous cell carcinoma of head and neck, 246
Cherubism: report of five new cases (ab), 664
Chest, deformities of anterior wall of (ab), 886
Children irradiated with small doses of roentgen rays, late results in, preliminary report (ab), 672
Cholangiographic medium, intravenous, new 5,5′-sebacoyl-diimino-bis (2,4,6-triiodo-N-methylisophthalamic acid), clinical evaluation of, preliminary report, 854
Cholangiography, percutaneous transhepatic, in differential diagnosis of jaundice (ab), 889
Cholecystography, renal insufficiency following, 859
Cholesteatoma, technique for study of middle ear; with special reference to, 1156
Chondrosarcoma of hand: report of case with radioactive sulphur studies and review of literature (ab), 220
Chromic oxide marker in absorption of fat, evaluation of (ab), 1117
Chronic cor pulmonale of thrombo-embolic origin, value of radioelectrokymography with automatic recording (or cinedensigraphy) in diagnosis of (ab), 443
Chyluria, demonstration of lymphatic abnormalities in patient with, 159
Cinefluorographic investigation of genitourinary tract function; bladder neck dysfunction, 1
Cinefluorography, pharyngeal, in clinical practice, 823
Cineroentgenographic frame enlarger, practical, to provide multiple "spot" roentgenograms, 176
"Cold regions" in thyroid-scintigrams (ab), 671
Collagen diseases, pulmonary changes seen in lung purpura and some of other (ab), 885
Colon associated with ulcerative and granulomatous colitis, roentgen findings in strictures of, 709
  diverticula of, milk in (ab), 1333
  manifestations, unusual, of lymphosarcoma; report of 2 cases (ab), 1333
Common bile duct lithiasis by sphincterotomy with sphincteroplasty, contribution of radiology to treatment of, report of four cases (ab), 211
Computers in dosimetry (E), 1088
Congenital anomalies and autosomal chromosome abnormalities, the relationship between (ab), 442
  heart disease, size of left atrium by x-ray examination in differentiation of interatrial and interventricular septal defects in (ab), 1329
Conray for angiography in patients with cerebrovascular disease, clinical evaluation of, 1281
Conversion ratio with ion exchange resin, determination of 24 hour protein bound radioiodine (PBI^{131}), 352
Corpus callosum, cerebral angiogram in agenesis of, 522
Corrosive gastritis, natural history of; report of five cases (ab), 1332
Cyst, peripelvic renal; case report with diagnostic roentgen sign, 81
Cystectomy, radical, for treatment of bladder cancer, experience with preoperative irradiation followed by, 1016
Cysts, fifty thoracic hydatid (ab), 885

Dachtler, Harry W.—last Charter Member of American Roentgen Ray Society (E), 1310
Damage to cervical spinal cord from therapeutic irradiation in neck region (ab), 217
  to ileum, unusual case of late post-irradiation (ab), 1116
Death following selective right ventricular angiocardiography; case report (ab), 1330
Deformities of anterior wall of chest (ab), 886
Deposition of radiant energy and initial radiochemical events, primary processes of, 896
Dermatomyositis with significant involvement of gastrointestinal tract, 746
Design and construction of new type isotope storage area, 404
Diencephalic pseudotumor effect, 1193
Disease, Morquio-Ullrich's: an inborn error of metabolism? (ab), 440
Diverticula, multiple ureteral; case report, 26
  of colon, milk in (ab), 1333
Diverticulum, intraluminal duodenal, 756
Divided-dose irradiation, office radiobiology and test of, 269
Dosimetry, computers in (E), 1088
  of fast electrons by means of condenser ionization chambers (ab), 672
Double contrast enema study (Malmö technique), rates and patterns of growth of 375 tumors of large intestine and rectum observed serially by, 673
Duodenal bulb, adenoma of; case report, 753
  diverticulum, intraluminal, 756
Dwarfism, ovarian, with pituitary tumor (ab), 213

Editorials
  The Sixty-fourth Annual Meeting of the American Roentgen Ray Society, 199
  Instruction Courses of the Sixty-fourth Annual Meeting of the American Roentgen Ray Society, 411
  The Language of Radiology, 656

  James Picker, 1882–1963, 659
  Gustav P. Bucky, M.D., 1899–1963, 661
  Some Aspects of Television Radiology, 871
  Manuel F. Madrazo, M.D., 1890–1963, 874
  Everett L. Pirkey, M.D., 1915–1963, 876
  Peter E. Russo, M.D., 1904–1963, 878
  Computers in Dosimetry, 1088
  The Sixty-fourth Annual Meeting of the American Roentgen Ray Society, 1302
  Sherwood Moore, M.D., 1880–1963, 1305
  A. Stanley Kirkland, M.D., 1890–1963, 1309
  Harry W. Dachtler—Last Charter Member of the American Roentgen Ray Society, 1310
ELECTRON MICROSCOPY, fine structure of bone as seen on fracture and cleavage planes by (ab), 1112
ELECTRONS, high-energy, using pencil beam scanning, radiation therapy with, 221
  high speed, radiation therapy with (ab), 670
EMPHYSEMA, perivesical (ab), 214
ENDOMETRIAL carcinoma, 1011
EPINEPHRINE on renal circulation, effect of; angiographic observations (ab), 1106
ESOPHAGEAL cancer; relationship to achalasia and hiatus hernia, diagnostic problem of, 778
  contraction ring, lower, anatomic basis for; plication theory and its applications, 811
  hiatus hernia, cancer of gastric cardia associated with (ab), 888
  hiatus hernia of stomach, 799
  ring, lower; long term follow-up of symptomatic and asymptomatic rings, 805
ESOPHAGUS, postoperative rupture of (ab), 887
ESTRADIOL 6, $7H^3$ in human being, vascular and extravascular radioactivity after injection of (ab), 1118
EVERETT L. PIRKEY, M.D., 1915–1963 (E), 876
EXCRETORY UROGRAPHY: comparison study of renovist and renografin 76 per cent, clinical evaluation of new medium for (ab), 1107
EXOPHTHALMOS response during roentgen therapy, 261
EXTRAHEPATIC TUMORS, liver scanning for, 1063
EXTRA-UTERINE PREGNANCY, radiological diagnosis of (ab), 1103
EXTRAVASATION near ureterovesical junction, 72

FAMILIAL METAPHYSEAL DYSPLASIA, Pyle's disease (ab), 219
FECAL EXCRETION of I^{131}; pitfall in interpretation of body scan, 1059
FETUSES, effects of radiocobalt irradiation of pregnant rabbits on development of (ab), 1118
FIBROSARCOMA occurring in draining sinus (ab), 1111
FISTULAE, internal biliary tract, 835
FISTULAS, demonstration of, by vaginography, 717
FRACTURE of lateral process of talus, 1277
  stress, with spondylolysis, 1258

GALLBLADDER, fixed filling defects of (ab), 890
  well opacified, and their evolution, study of fixed filling defects in, 844
GALLSTONE intestinal obstruction, operative and radiologic relief (ab), 211
GAMMA CAMERA in investigation of thyroid disorders, use of, 345
GAS-GANGRENE, circumscribed, abscess of brain: case report together with account of literature (ab), 665
GASTRIC CARDIA, cancer of, associated with esophageal hiatus hernia (ab), 888
GASTROESOPHAGEAL retrograde mucosal prolapse; cause of upper gastrointestinal hemorrhage, 774
GASTROINTESTINAL trace, dermatomyositis with significant involvement of, 746
GENITOURINARY TRACT function, bladder neck dysfunction, cinefluorographic investigation of, 1
GLIOMA, vascularized malignant, and intracranial arteriovenous malformation, angiographic differential diagnosis between, 512
GLIOMAS, hemispheric, widened septum pellucidum in (ab), 666
GLOMERULONEPHRITIS, roentgenographic appearance of pulmonary hemorrhage associated with, 83
GOITER, simple, defective deiodination of I^{131}-labeled L-diiodotyrosine in patients with (ab), 1117
GUSTAV P. BUCKY, M.D., 1899–1963 (E), 661
GYNECOLOGY and obstetrics, percutaneous transfemoral aortography in (ab), 212
  lymphangiography in (ab), 212

HARRY W. DACHTLER—last Charter Member of the American Roentgen Ray Society (E), 1310
HEAD and neck, dosage to important sites in radiation therapy of tumors about, 240
HEMANGIOMATOSIS, intestinal and cutaneous; report of case (ab), 211
HEMATOMA, extradural, roentgenologic aspects of, 462
  intramural of jejunum; case report, 732
HEMATOMAS, unilateral and bilateral, angiographic features of convexity subdural hematomas with emphasis on differential diagnosis between, 445
HEMIHYPERTROPHY, congenital: review of literature and report of case with special emphasis on oral manifestations (ab), 442
HEMOLYTIC STREPTOCOCCUS, pneumonia caused by (ab), 667
HEMORRHAGE, pulmonary, associated with glomerulonephritis, roentgenographic appearance of, 83
HEPATIC ARTERY, aneurysm of; importance of angiographic visualization, 578
HEREDITARY TRANSMISSION of congenital coalition of calcaneus to navicular (ab), 1110

Hiatal hernia, criteria for diagnosis of (ab), 887
High energy electromagnetic radiation, the relative surface ionization for, 231
Histoplasmosis, chronic cavitary, of lung (ab), 885
Hodgkin's disease, early, role of chemotherapy in management of, 968
  relationship of histologic features to clinical stages in, 944
Humeral epiphysis, distal, displacement of, in newborn infant (ab), 219
Hydatid cysts, thoracic, fifty (ab), 885
Hydronephrosis due to aberrant blood vessels versus communicating peripelvic cysts; roentgenographic diagnosis, 109
Hyperthyroidism, radioiodine in diagnosis and therapy of (ab), 1116
Hypopharynx carcinoma, treatment of cervical lymph node metastases from, 997
Hytrast, bronchographic crystalline-inclusion pneumonia due to (ab), 1101

I^{131}, fecal excretion of; pitfall in interpretation of body scans, 1059
  -labeled L-diiodotyrosine in patients with simple goiter, defective deiodination of (ab), 1117
Idiopathic scoliosis in fraternal twins (ab), 1108
Image-forming quality of radiographic screen-film systems: line spread-function, 178
Infancy, total body opacification in conventional and high dose intravenous urography, in, 63
Infantile cortical hyperostosis presenting with exophthalmos: case report (ab), 1108
Infants, acute perforation in (ab), 1334
Instruction Courses of Sixty-fourth Annual Meeting of American Roentgen Ray Society (E), 411
Insula and deep middle cerebral venous drainage system: normal anatomy and angiography, 472
Interstitial and intracavitary radiation therapy, afterloading in, 386
Intestinal hemorrhage, pancreatic cystadenoma with, 735
  obstruction, gallstone, operative and radiologic relief of (ab), 211
Intracavitary radiation therapy, afterloading in interstitial and, 386
Intraspinal foreign bodies, case report of (ab), 216
Iodine 125 in thyroid scintiscanning, use of, 1052
Ionization, the relative surface, for high energy electromagnetic radiation, 231
Irradiated cells, biochemical basis of reproductive death in, 907
Irradiation and chemotherapy, combined, in treatment of squamous cell carcinoma of head and neck, 246
  and surgery, for advanced cancer of laryngopharynx, combined therapy, 1023
  test of divided-dose, office radiobiology and, 269
Isotope renogram in carcinoma of cervix; preliminary report, 149
  storage area, design and construction of new type, 404

James Picker, 1882–1963 (E), 659
Jejunum, intramural hematoma of; case report, 732

Kidney, injuries in childhood, significance of selective renal angiography in, 75
Kirkland, A. Stanley, 1890–1963 (E), 1309

Language of radiology (E), 656
Laryngeal cancer, end results of treatment of cervical metastases, 1004
Laryngopharynx, combined therapy, irradiation and surgery, for advanced cancer of, 1023
Leukemia, chronic lymphocytic, long term experiences with use of P^{32} in treatment of (ab), 672
Leukoencephalopathy, progressive multifocal (ab) 1115
Limbs, causes of uneven length (ab), 440
Liver scanning for extrahepatic tumors, 1063
Lumbar vertebra, Paget's disease confined to one, 1271
Lumbosacral retrodisplacement, 1263
Lung, chronic cavitary histoplasmosis of (ab), 885
  purpura and some of other collagen diseases, pulmonary changes seen in (ab), 885
Lymphangiography, experiences with (ab), 1113
  in cobalt teletherapy of certain neoplasms, advantages of (ab), 441
  in gynecology (ab), 212
  oil embolism in: incidence, manifestations, and mechanism (ab), 1113
  simple injector for (ab), 1113
Lymphatic abnormalities in patient with chyluria, demonstration of, 159
  and vascular system of dogs, experimental approach in use and magnetic control of metallic iron particles as contrast and isotopic agent in, 1068
Lymphography, "second-look," 1078
Lymphomas, early, contribution of radiation therapy in control of, 956
  introduction to symposium on, 938
  malignant, following local treatment, course of Stage I, 939
  malignant, of skin, effect of radiation therapy on prognosis of (ab), 669
  use of radioactive isotopes in treatment of, 311
Lymphosarcoma, unusual colon manifestations of; report of 2 cases (ab), 1333

Madrazo, Manuel F., M.D., 1890–1963 (E), 874
Malformations, drug-induced (thalidomide) (ab), 213
Malignancy, pelvic, intraosseous venography in, 373

- (MALMÖ TECHNIQUE), rates and patterns of growth of 375 tumors of large intestine and rectum observed serially by double contrast enema study, 673
- MAMMOGRAPHY: a study of 500 patients, 366
  - experience with 366 cases at Columbia Hospital for Women (ab), 443
  - reproducibility of; preliminary report, 356
- MANUEL F. MADRAZO, M.D., 1890–1963 (E), 874
- MATERNAL CIRCULATION in placenta of rhesus monkey; radioangiographic study, 638
- MEDIAN NERVE COMPRESSION to Sudeck's syndrome, relation of (ab), 1110
- MELANOMA problem, newer view of (ab), 669
- MELANOMAS, malignant, of skin, radiation therapeutic advances and results in (ab), 669
- MENINGOCELE, lateral intrathoracic; case report with preoperative diagnosis, 1216
- MESENTERIC ADENITIS, roentgen manifestations of, 727
- METALLIC IRON PARTICLES in lymphatic and vascular system of dogs as contrast and isotopic agent, experimental approach in use and magnetic control of, 1068
- METASTASES, calcified, in liver from primary gastric carcinoma: with discussion of question of calcium deposition in mucin producing carcinomata (ab), 1336
- MIDDLE cerebral venous drainage system, deep, and insula: normal anatomy and angiography, 472
  - ear and mastoid process, normal and pathologic roentgen anatomy of, 1143
  - ear, with special reference to cholesteatoma, technique for study of, 1156
- MITRAL REGURGITATION (ab), 1329
- MOORE, SHERWOOD, 1880–1963 (E), 1305
- MORQUIO-ULLRICH'S DISEASE: an inborn error of metabolism (ab), 440
- MUSTINE THERAPY, high-dose, for bronchial carcinoma (ab), 670
- MYELOMENINGOCELE, paralytic luxation of hip in (ab), 217
- MYOCARDIAL INFARCTION, roentgen diagnosis of pulmonary embolism and its differentiation from, 632

- NAVEL SHADOW (ab), 443
- NEPHROGRAM EFFECT in excretory urography, time of maximum (ab), 215
- NEPHROGRAPHY, radio-isotope (ab), 214
- NEPHROTOMOGRAPHY in urologic diagnosis, evaluation of, 115
- NEWBORN INFANT, displacement of distal humeral epiphysis in (ab), 219

- ODONTOGENIC MAXILLARY SINUSITIS; case reports and radiologic considerations (ab), 664
- OESOPHAGEAL ATRESIA, unusual variation of (ab), 1331
- OFFICE RADIOBIOLOGY and test of divided-dose irradiation, 269
- OIL EMBOLISM in lymphangiography: incidence, manifestations, and mechanism (ab), 1113
- ONCOLYSIS ENHANCEMENT: plasma constituents produced by whole body irradiation; further studies on, 300
- ORAGRAFIN, new cholecystographic medium; double-blind comparison with telepaque (ab), 1102
- ORAL CANCER, cervical lymph node involvement in, 978
- OROPHARYNGEAL CARCINOMA, metastases in cervical lymph nodes from; treatment and results, 990
- OSTEOARTHROPATHY, patent ductus arteriosus and (ab), 886
- OSTEOFIBROSIS DEFORMANS JUVENILIS, roentgen observations in diagnosis and differential diagnosis of (ab), 218
- OSTEOID OSTEOMA of spine (ab), 1110
- OSTEOMYELITIS of thoracic spine, displacement of linear thoracic paraspinal shadow of Brailsford; early sign in, 1231
- OSTEOPHYTOSIS and syndesmophytosis (ab), 1109
- OSTEOPOROSIS CIRCUMSCRIPTA, pituitary insufficiency following meningitis; report of case with roentgenographic signs simulating, 1167
- OVARIAN DWARFISM with pituitary tumor (ab), 213

- P^{32}, determination of distribution of, in phantoms and in patients by detection of Bremsstrahlung radiation with scintiscanner, 325
  - in treatment of chronic lymphocytic leukemia, long term experiences with use of (ab), 672
- PAGET'S DISEASE confined to one lumbar vertebra, 1271
  - disease (osteitis deformans) of pelvis, brim sign; new sign found in, 1267
- PANCREAS, annular, in infancy; report of 3 cases, 740
- PANCREATIC CYSTADENOMA with intestinal hemorrhage, 735
- PANTOPAQUE ANTERIOR BASAL CISTERNOGRAPHY of posterior fossa, 1197
- PARALYTIC LUXATION of hip in myelomeningocele (ab), 217
- PATENT DUCTUS ARTERIOSUS and osteoarthropathy (ab), 886
- PELVIC disease, illustration of approach to diagnosis of (ab), 1104
  - malignancy, intraosseous venography in, 373
- PENIS, lesions of, application of cavernosography in diagnosis of, 169
- PERFORATION, acute, in infants (ab), 1334
- PERICARDITIS with effusion in infants and children (ab), 1330
- PERITONEAL SAC, lesser, radiological observations on (ab), 1335
- PERIVESICAL EMPHYSEMA (ab), 214
- PETER E. RUSSO, M.D., 1904–1963 (E), 878

- PHARYNGEAL CINEFLUOROGRAPHY in clinical practice, 823
- PHOCOMELIA AND INTERNAL DEFECTS due to thalidomide (ab), 213
- PHOTOSCANS, color television contrast expansion of, 406
- PHYSIOLOGY OF SMALL BLOOD VESSELS, acute effects of radiations on, 294
- PICKER, JAMES, 1882–1963 (E), 659
- PIRKEY, EVERETT L., M.D., 1915–1963 (E), 876
- PITUITARY fossa, new standard for size of (ab), 667
  - insufficiency following meningitis; report of case with roentgenographic signs simulating osteoporosis circumscripta, 1167
  - tumor with ovarian dwarfism (ab), 213
- PLACENTAL LOCATION and circulation, radioisotope (I^{131}) studies of (ab), 1103
- PLASMOCYTOMA, clinical and radiologic study of, (considerations of 43 cases) (ab), 1111
- PLEURAL EFFUSION, shape of (ab), 886
- PLICATION THEORY and its applications; anatomic basis for lower esophageal contraction ring, 811
- PNEUMOENCEPHALOGRAPHY and autotomography, improved chair for, 184
  - convenient, 1205
- PNEUMOCEPHALUS, traumatic, 1171
- PNEUMONIA, bronchographic crystalline-inclusion, due to hytrast (ab), 1101
  - caused by hemolytic streptococcus (ab), 667
- POLYMYOSITIS: report of two cases with pulmonary function studies suggestive of progressive systemic sclerosis (ab), 1114
- PONTICULUS POSTICUS of first cervical vertebra between ages six to seventeen, incidence of (ab), 667
- PORTABLE RADIOACTIVE SOURCES, some new, for diagnostic radiography, 1123
- PORTACAVAL SHUNTS, qualitative and quantitative estimate of (ab), 441
- POSITRON-EMITTING As^{74}, radioencephalographic scanning with, 336
- POSTERIOR FOSSA, dermoid tumor of, associated with congenital dermal sinus (ab), 666
  - pantopaque anterior basal cisternography of, 1197
- POSTMYOCARDIAL INFARCTION SYNDROME, 628
- POSTSTENOTIC AORTIC DILATATION as roentgen sign in congenital valvular aortic stenosis, 571
- POST-TRAUMATIC DIAPHRAGMATIC HERNIAS and eventrations, refinements of technique for radiologic diagnosis of (ab), 1331
- PRELIMINARY PROGRAM; Sixty-fourth Annual Meeting of American Roentgen Ray Society, 201
- PRESIDENT'S ADDRESS, 893
  - Preservation of Image, 1121
- PROTEIN BOUND RADIOIODINE (PBI^{131}) conversion ratio with ion exchange resin, determination of 24 hour, 352
- PROTRUSIO ACETABULI in childhood (ab), 1110
- PSEUDOGOUT (articular chondrocalcinosis); analysis of 20 cases, roentgenographic aspects of, 1248
- PULMONARY artery and branches, roentgenologic features of single and multiple coarctations of, 599
  - artery, asplasia of (ab), 1101
  - changes seen in lung purpura and some of other collagen diseases (ab), 885
  - circulation, systemic, angiography of, 614
  - embolism and its differentiation from myocardial infarction, roentgen diagnosis of, 632
  - hemorrhage associated with glomerulonephritis, roentgenographic appearance of, 83
  - venous obstruction, severe, in total anomalous pulmonary venous connection to left innominate vein; report of case, 593
- PYELOGRAM, intravenous, effect of (voluntary) bladder distention on; experimental study, 37
  - minute sequence, 55
- PYELONEPHRITIS, tumefactive xanthogranulomatous, 89
  - xanthogranulomatous, 97
- PYLE'S DISEASE, familial metaphyseal dysplasia (ab), 219

- RADIANT ENERGY and initial radiochemical events, primary processes of deposition of, 896
- RADIATION effects at tissue and tumor level, quantitative aspects of, 928
  - lethality at cellular level, quantitative aspects of, 917
  - therapy, afterloading in interstitial and intracavitary, 386
  - therapeutic advances and results in malignant melanomas of skin (ab), 669
  - therapy of tumors about head and neck, dosage to important sites in, 240
  - therapy on prognosis of malignant lymphomas of skin, effect of (ab), 669
  - therapy with high-energy electrons using pencil beam scanning, 221
  - therapy with high speed electrons (ab), 670
- RADIATIONS, acute effects of, on physiology of small blood vessels, 294
- RADIOACTIVE isotopes, use of, in treatment of lymphomas, 311
  - sulphur studies and review of literature, report of case of chondrosarcoma of hand (ab), 220
- RADIOBIOLOGY, office, and test of divided-dose irradiation, 269
- RADIOCOBALT IRRADIATION of pregnant rabbits on development of fetuses, effects of (ab), 1118
- RADIOELECTROKYMOGRAPHY with automatic recording (or cinedensigraphy) in diagnosis of chronic cor pulmonale of thrombo-embolic origin, value of (ab), 443

Radioencephalographic scanning with positron-emitting As^{74}, 336

Radiographic changes in bony trabecular pattern in mandible of growing Macaca rhesus monkeys following condylar resection (ab), 667
  diagnosis of thymic tumors (ab), 1101
  mottle, spatial fluctuations of x-ray quanta and recording of, 863
  screen-film systems, image-forming quality of; line spread-function, 178

Radiography, advantages of three-phase spot-film (ab), 1115
  some new portable radioactive sources for diagnostic, 1123
  subtraction, simple method of (ab), 443

Radioiodine in diagnosis and therapy of hyperthyroidism (ab), 1116
  malignant bone pain relief with (ab), 671
  uptake studies in newborn infants (ab), 670

Radioisotope (I^{131}) studies of placental location and circulation (ab), 1103
  nephrography (ab), 214
  renogram in renovascular hypertension, accelerated vascular phase of, 135
  renogram test, *in vitro* analysis of (ab), 215

Radiologic aspects of thallium poisoning (ab), 1336
  examination: comparison of techniques, bowel preparation for (ab), 888
  features of acute massive adrenal hemorrhage of newborn (ab), 216

Radiological diagnosis of extra-uterine pregnancy (ab), 1103
  observations on lesser peritoneal sac (ab), 1335

Radiology, language of (E), 656
  of post-operative abdomen (ab), 1335
  television, some aspects of (E), 871

Radiopaque injection of thoracic duct: morphologic and functional observations on lymphatic circulation when subphrenic and mediastinal lymph nodes are blocked by neoplastic involvement (ab), 1112

Radiorenogram, effects of apprehension, 141
  tubular loading as means of improving, 157

Radiotherapy in treatment of patients with seminomas and teratomas of testicle (ab), 668
  split-dose: follow-up in 50 cases, 280

Radium capsules for radon leakage, testing, 396
  sources, simple test for leaking, 403
  toxicity, unusual case of, 1042

Recklinghausen's disease, orbital, cranial and facial manifestations of plexiform neuroma of (ab), 665

Reiter's syndrome (ab), 1114

Renal angiography in injuries of kidney in childhood, significance of selective, 75
  arteries, multiple, roentgenologic evaluation of, 583
  arteriography (aortography) a reliable test in differential diagnosis between kidney cysts and neoplasms, is? (ab), 1105
  arteriography, selective, 124
  circulation, effect of epinephrine on; angiographic observations (ab), 1106
  cyst, peripelvic; case report with diagnostic roentgen sign, 81
  disease, unilateral, in patients with hypertension, ^{131}I-"Hippuran" renography in detection of (ab), 1107
  insufficiency following cholecystography, 859
  papillary necrosis (ab), 1104
  tumors, renal angiography by retrograde femoral catheterization as aid to diagnosis of (ab), 1105

Renogram test, *in vitro* analysis of radioisotope (ab), 215

Renovascular hypertension, accelerated vascular phase of radioisotope renogram, 135
  excretory urography in diagnosis of; methods of enhancing its value (ab), 1106

Reproducibility of mammography; preliminary report, 356

Retrodisplacement, lumbosacral, 1263

Retrotracheal lymphadenopathy in bronchial carcinoma, revealed by barium-filled esophagus, 792

"Ring" shadow in diagnosis of ulcer, 767

Roentgen diagnosis of pulmonary embolism and its differentiation from myocardial infarction, 632
  diagnosis of ureterocele in children, 15
  findings in strictures of colon associated with ulcerative and granulomatous colitis, 709
  manifestations of mesenteric adenitis, 727
  manifestations of subclavian steal syndrome, 528
  rays, late results in children irradiated with small doses of, preliminary report, (ab), 672
  sign in congenital valvular aortic stenosis, post-stenotic aortic dilatation as, 571
  therapy, exophthalmos response during, 261

Roentgenographic aspects of pseudogout (articular chondrocalcinosis); analysis of 20 cases, 1248
  visualization of human testicular lymphatics; preliminary report (ab), 216

Roentgenography of breast, soft tissue; analysis of factors which influence roentgenographic quality and description of new technique, 359
  wide angle, 189

Roentgenologic aspects of extradural hematoma, 462
  evaluation of multiple renal arteries, 583
  features of single and multiple coarctations of pulmonary artery and branches, 599

Rupture, postoperative, of esophagus (ab), 887

Russo, Peter E., M.D., 1904–1963 (E), 878

Sarcoidosis of skull (ab), 665

Sarcoma, synovial, observations on (ab), 1111

Scanning, pencil beam, radiation therapy with high-energy electrons using, 221
Schistosomiasis mansoni: roentgenologic observations in nonendemic area, 688
5,5′-Sebacoyl-diimino-bis (2,4,6-triiodo-N-methyl-isophthalamic acid), preliminary report, clinical evaluation of new intravenous cholangiographic medium, 854
"Sephadex chromatographic" test in evaluation of thyroid function (ab), 671
Septum pellucidum, widened, in hemispheric gliomas (ab), 666
Sherwood Moore, 1880–1963 (E), 1305
Sinus, congenital dermal, dermoid tumor of posterior fossa associated with (ab), 666
Sixth-fourth Annual Meeting of American Roentgen Ray Society (E), 1302
Skull, sarcoidosis of (ab), 665
Small bowel barium motor meal, evaluation of; with emphasis on effect of volume of barium suspension ingested (ab), 1332
  with intravenously administered contrast medium, opacification of (ab), 1332
Sodium iothalamate, angio-conray, in selective angiography; further evidence of low toxicity, 1287
Spatial fluctuations of x-ray quanta and recording of radiographic mottle, 863
Sphincterotomy with sphincteroplasty, contribution of radiology to treatment of common bile duct lithiasis by; report of four cases (ab), 211
Spinal blocks, late, after tuberculous meningitis, 1220
  extradural cysts; with report of ossified spinal extradural cyst, 1227
Spine, osteoid osteoma of (ab), 1110
Split-dose radiotherapy: follow-up in 50 cases, 280
Spondylolysis, stress fracture with, 1258
Spondylosis, lumbar, with compression of cauda equina (ab), 440
"Spot" roentgenograms multiple, practical cineroentgenographic frame enlarger to provide, 176
Staphylococcic infection in infants and children, unusual manifestations of (ab), 1114
Stomach, esophageal hiatus hernia of, 799
Strontium-85, use of, in evaluation of bone metastases: preliminary report (ab), 671
Subclavian steal syndrome, 532
  clinical and roentgenographic aspects of, 535
  roentgen manifestations of, 528
Sudeck's syndrome, relation of median nerve compression to (ab), 1110
Supervoltage radiation therapy in advanced cancer of urinary bladder (ab), 1115
Surgery and irradiation, combined therapy, for advanced cancer of laryngopharynx, 1023
Sympathicoblastoma: radiological findings in forty-three cases (ab), 217
Syndesmophytosis and osteophytosis (ab), 1109
Syndrome, postmyocardial infarction, 628
Synostosis, talonavicular (ab), 220
Synovial sarcoma, observations on (ab), 1111
Syringomyelia, remarkable skeletal changes in (ab), 218

Talonavicular synostosis (ab), 220
Talus, fracture of lateral process of, 1277
Tannic acid in barium, enema lethal effects of; report of three fatalities and experimental studies, (ab), 1335
Television, color, contrast expansion of photoscans, 406
  radiology, some aspects of (E), 871
  X-ray image storage apparatus, 1290
Testicle, radiotherapy in treatment of patients with seminomas and teratomas of (ab), 668
Testicular lymphatics, human, roentgenographic visualization of; preliminary report (ab), 216
Testis, tumors of (ab), 668
  tumours of, some pathological considerations (ab), 444
Thalidomide, drug-induced malformations (ab), 213
  phocomelia and internal defects due to (ab), 213
Thallium poisoning, radiologic aspects of (ab), 1336
Therapeutic irradiation in neck region, damage to cervical spinal cord from (ab), 217
Thoracic duct, radiopaque injection of: morphologic and functional observations on lymphatic circulation when subphrenic and mediastinal lymph nodes are blocked by neoplastic involvement (ab), 1112
Three-phase spot-film radiography, advantages of (ab), 1115
Thyroid disorders, use of gamma camera in investigation of, 345
  function, "sephadex chromatographic" test in evaluation of (ab), 671
  scintigrams, "cold regions" in (ab), 671
  scintiscanning, use of iodine 125 in, 1052
Tissue, soft, diagnosis with CO$_2$-insufflation (ab), 443
Trauma to ureter, 28
Traumatic pneumocephalus, 1171
Tuberculoma of brain, 1185
Tuberculous meningitis, late spinal blocks after, 1220
Tubular loading as means of improving radiorenogram, 157
Tumor, dermoid, of posterior fossa associated with congenital dermal sinus (ab), 666
Tumors about head and neck, dosage to important sites in radiation therapy of, 240
  mucous gland, histology, natural history and re-

sults of treatment of, 1032
- 375, of large intestine and rectum observed serially by double contrast enema study (Malmö technique), rates and patterns of growth of, 673
- thymic, radiographic diagnosis of (ab), 1101

TUMOURS of testis (ab), 668
- of testis-some pathological considerations (ab), 444

TWINS, fraternal, idiopathic scoliosis in (ab), 1108

ULCER, Billroth-I recurrent (ab), 888
- "ring" shadow in diagnosis of, 767

URETER, trauma to, 28

URETERAL DIVERTICULA, multiple; case report, 26
- stump reflux, demonstration of, by voiding cystourethrography during excretory pyelography (ab), 1108

URETEROCELE in children, roentgen diagnosis of, 15

URETEROVESICAL JUNCTION, extravasation near, 72

UROGRAPHY, excretory, time of maximum nephrogram effect in (ab), 215
- in infancy, total body opacification in conventional and high dose intravenous, 63

UROLOGIC diagnosis, evaluation of nephrotomography of, 115

VAGINOGRAPHY, 721
- demonstration of fistulas by, 717

VASCULAR LESIONS of female pelvis: with report of aneurysm with arteriovenous fistula of uterine artery and vaginal vein (ab), 1103

VENOGRAPHY, intraosseous, in pelvic malignancy, 373

VENTRICULAR SPAN in cerebral pneumography, 1176

VERTEBRAL epiphysitis: comparison of clinical and roentgenologic findings, 1236
- pedicle, congenital deficiency of (ab), 1109

VOLVULUS, organo-axial gastric, acute, 761

WHIPPLE'S DISEASE with associated splenomegaly and pancytopenia (ab), 1333

WHOLE BODY IRRADIATION, plasma constituents produced by: further studies on oncolysis enhancement, 300

XANTHOGRANULOMATOUS PYELONEPHRITIS, 97
- tumefactive, 89

X-RAY quanta and recording of radiographic mottle, spatial fluctuations of, 863
- television image storage apparatus, 1290

AUTHOR INDEX TO VOLUME 90

*=Original Article

Abbasoglu, Semir, 1103
Abrams, Herbert L., 1106, 1113
Acar, J., 443
Ackerman, L. V., *673
Adeney, N. F., 1105
Albert, Solomon N., 887
Aldana, A. Luis, 1336
Alexander, L. L., 671
Allain, Y., 1331
Altman, Robert S., 666
Amplatz, Kurt, *184
Andersen, Howard A., 885
Anderson, M. Sidney, 1335
Anlyan, William G., 889
Arcomano, Joseph P., 890
Ariel, Irving M., *311
Arnold, H. R., *628
Asch, Thane, *366
Ashby, Robert N., *535, *564
Atallah, Naim K., *740
Atkinson, R. James, *1078
Avnet, Norman L., *89

Bailey, R. W., 1108
Bailey, Robert W., 1108
Baird, Robert M., *546
Baker, William H., 211
Bank, S., 1332
Barborka, C. J., 887
Barnett, James C., 890
Barrett, A. F., 217
Barton, Evan M., 1114
Bartone, Noel F., *844
Bauer, Raymond B., *490
Baum, Stanley, 1113
Baylin, G. J., *157
Baylin, George J., *141
Beall, Arthur C., Jr., *1281
Behrens, D., 1336
Beierwaltes, William H., *261
Bennett, David, 659
Benson, Ralph C., 212
Berci, George, *1290
Bergmann, Karl, 888
Berlin, Herbert S., *189
Berlin, Leonard, *1185
Bernard, P., 665
Biggs, Norman L., 667
Birkbeck, J. A., 670
Blackstone, Dewey P., *176
Bladin, P., 666
Blady, John V., *1004
Blahut, Robert J., *261
Bloch, Claude, *709
Bloomberg, Gordon R., 1335
Boag, John W., *896
Bobbio, P., 441
Bocara, S., 664
Bock, K., 1101
Boijsen, Eric, 1106
Bonneau, M., 664
Bonnin, N. J., 1104
Boone, John A., 1329
Borgström, Karl-Erik, 1106
Born, James L., 672
Borrie, John, 885
Bose, K. S., 1111
Bourdet, P., 1331
Bourthomieux, A., 443
Bouvrain, Y., 443
Boyd, John R., 213
Boyer, Carl W., Jr., *753
Brachfield, Karel, 672
Brandt, Ira K., 442
Brannan, Harold M., *83
Bron, Klaus M., 1113
Bronstein, Eugene L., *1016
Brown, A. S., 885
Brown, V. St. J., 216
Buchwald, W., 443
Bühlmann, A., 441
Bundesen, W. E., 887
Bur, Grato E., 1118
Burge, C. H., 1107
Burger, Robert, 1104
Burhenne, H. Joachim, *1176
Burmeister, R. W., 667
Burnett, L., *240
Burns, Robert R., *614
Busch, Frederick M., 216
Bywaters, T. W., Jr., 1108

Caldwell, William L., 1332
Campbell, James M., 1115
Canino, Christopher W., *835
Cannon, Abram H., 214, *535, *564
Căpek, V., *75
Caplan, Lawrence, *149
Capp, M. Paul, 889
Carey, Lewis S., *593
Carpender, J. W. J., *221
Carroll, C. J., 1108
Caulk, Ralph M., 199, *1121
Cayler, G. G., 1330
Chait, Arnold, *688
Chandler, Arthur, *1216
Chang, M. C., 1118
Charkes, N. David, *406, *1052
Chejfe, G., 887
Chesledon, Wayne A., 443
Cheung, O. T., 885
Chowdhuri, B., 1111
Chvojka, V. E., 887
Chynn, Kuo York, *554
Ciccalese, Gerald, 1103
Cimmino, Christian V., *1277
Clamen, Marvin, 1116
Clausen, J., 440
Climie, A. R. W., *735
Coe, Fred O., *721
Collica, Carl J., *352
Connolly, P. J., *735
Conte, Mario, *578
Cook, Galen B., *723
Cooperman, L. R., 1102
Corbin, Leon J., *189
Corner, George W., Jr., *638
Corry, D. C., 1333
Cosgriff, Stuart, *859
Cravitz, Barbara, *1052
Crawford, Stanley, *1281
Cronic, Francis, *1068
Cross, Lawrence C., *1143
Crummy, A. B., 1102
Culver, Gordon J., *732

Daly, John F., *246
Dann, D. S., *717
Daugherty, Guy W., 885
Davies, Alan, 890
Davies, H., 666
Davies, Hugh, *1176
Davis, George D., *583
Davis, Stanley, 886
Daywitt, Alvin L., *1171
De Bakey, Michael E., *1281
Dechaume, M., 664
Decker, John L., 1114
Delahaye, R. P., 1331
DeMaria, W. J. A., *157
DeMaria, William J. A., *141
Denham, R. H., Jr., 1111
Derow, Joshua R., *1227
Dewey, William C., *325
Deyton, Walter E., *55
Dingley, A. F., Jr., 1111
Dinsmore, R., 1329
Dische, Stanley, *149
Dixon, Andrew D., 1118
Dodd, Gerald, *169, 212
Dodson, Vernon N., 215
Doig, A., 1107, 1107
Dolman, C. L., 213
Donald, K. W., 1107
Donner, Martin W., *638
Doppman, John, *578

Dotter, Charles T., 212, *571, *650, 1330
Dragoni, G., 1111
Draper, John W., 1104
Dukes, Herbert T., *512
Dunbar, J. S., *37, 216
Duncan, J. G., 1335
Dyggve, H. V., 440

Edmond, Beauvoir, *1193
Edwards, Jesse E., *593
Effler, Donald B., 888
Egan, Robert L., *356
Eichler, J., 218
Elkin, Milton, *28
Emmett, John L., *115
Epperson, Robert D., *1
Epstein, Bernard S., 1109
Epstein, Joseph A., 1109
Ernst, Helmut, 671
Etter, Lewis E., 656, *1143
Evans, Robley D., *396
Evans, T. C., 670

Fagan, Charles J., *774
Fagan, W. T., 1113
Farman, J., 1332
Feldman, Frieda, *746
Fergusson, J. D., 668
Fetter, Theodore R., *169
Fields, William S., *1281
Fierst, Sidney M., 1117
Figiel, Leo A., *761
Figiel, Steven J., *761
Finby, Nathaniel, *159, 1104
Fine, David I. M., *522
Fineberg, C., 1103
Finkel, A. J., *1042
Fischer, Martin J., *532
Fleischner, Felix G., *792
Flemma, Robert J., 889
Fletcher, Gilbert H., *893, *990
Floch, Martin H., 1332
Flood, Charles A., *778
Foxworthy, Donald T., 1114
Fraser, G. A., 1105
Freimanis, Atis K., *445
Friedenberg, Marvin J., *97
Friedenberg, Richard M., *28, *72
Friedenberg, Z. B., 1110
Friedman, A. B., 671
Friedman, Milton, *246
Fojtík, F., *75
Franch, Robert H., *599

Gabriel, James B., 1117
Gallaghar, Robert G., *396
Gardner, Clarence E., Jr., 889
Gardner, Frances, 886
Gass, Harvey, *1197
Gavalà, S., 216
Gay, Brit B., Jr., *599
Gershon-Cohen, J., *406
Gilroy, John, *490
Gleason, Donald M., 215
Glenn, James F., *55
Goffrini, Piero, 1112
Gold, Sandra, *294
Goldberg, Herbert R., *89
Goldman, Joseph L., *1023
Goldman, K. P., 670
Good, C. Allen, *83
Goree, John A., *512
Gorlin, Robert J., 442
Gottschald, Raymond G., 220
Grabstald, Harry, *1016
Grainger, Ronald G., 1101
Gras, François, 211
Green, Farno L., *1123
Green, Robert A., 1115
Greene, Laurence F., *115
Greenspan, Richard H., 1115
Grellet, M., 664
Grieco, R. Vincent, *844
Griem, M. L., *221
Groves, Laurence K., 888
Grunfeld, G. Oscar, 1336
Guilbert, F., 664
Guiss, Lewis W., *997

Hadley, Lee A., *1258
Hahn, George A., 212
Hall, Charles A., *404
Hall, P., 1114
Halpern, Mordecai, *124, *528
Hargraves, Malcolm M., 885
Harvey, Elmer B., 1118
Hashim, Sami, *159
Haskin, Marvin E., *1248
Hasterlik, R. J., *1042
Headington, John T., 1115
Heagy, Fred C., 1103
Heidelberg, Joan G., *325
Helfrich, Richard B., *753
Hellriegel, Werner, 668, 669
Helock, Tina, *1052
Henschke, Ulrich K., *386
Herbst, M., 1101
Herndon, C. Nash, 1110
Heroy, William W., 890
Herrera, Pedro Medina, 214
Herzberger, Eugene E., *1216
Hess, Dieter, 669
Hess, Paul, 669
Hilaris, Basil S., *386
Hinostroza, O. Gerardo, 1336
Holsti, Paul, 669
Holsti, Lars R., 669
Holtzman, R. B., *1042
Howarth, J. L., *231
Hoyte, David A. N., 1118
Huang, Yun Peng, *472
Hunt, Dorothy M., 1118
Hunt, James C., *583
Hustu, Omar, *1016

Isley, Joseph K., Jr., * 141

Jackson, Laird, 212
Jacobs, Lewis G., 1116
Jacobson, G., 1329
Jacobson, Harold G., *189
Jaedke, W., 1336
Jakoubkova, Jaroslavá, 672
Jeffreys, T. E., 1111
Jesse, R. H., *990
Johnson, Philip, 671
Johnson, R. E., *673
Johnston, David O., *373
Johnston, Robert F., 1115
Juhl, J. H., 1102

Kahn, Robert J., *1171
Kane, John J., 1329
Kaplan, Henry S., *907
Karck, G., 218
Karnofsky, David A., *968
Karras, Bill Gust, *564
Karras, Bill G., 214, *535
Kaufman, Joseph J., *26, 1106
Keats, Theodore E., *359
Kelly, Luther W., Jr., 213
Kendrick, George S., 667
Khanna, S. R., 667
Kim, Tak Ki, 1110
Kincaid, Owings W., *583
Kittredge, Richard D., *159, 1104
Kling, George A., 871
Knight, I. C. S., 1107
Koenig, Elizabeth Ulman, 442
Koenig, George F., *359
Kofman, Sidney, 671
Kolár, Jaromír, 672
Kozlowski, Kazimierz, *1220
Krabbenhoft, Kenneth L., *490, *1123, 1302
Kramer, Simon, *149
Kratochvil, L., 219
Krause, George R., *767
Krueger, R., *157
Krueger, Thomas P., *506
Kusakabe, Tunesuke, 1117

Lamarque, J. L., 441
Lamarque, P., 441
Lambie, R. W., *717
Lampe, Isadore, *261, *1011
Lang, Erich K., 1105
Lanzi, L. H., *221
Lapayowker, Marc, *546

Larson, Sanford J., *1193
Lattimer, John K., 1105
Laudan, J. C. H., *756
Laur, A., *632
Lavine, Leroy S., 1109
Lawrence, J. R., 1107, 1107
Lawrence, John H., 672
Lécutier, M. A., 213
Le Genissel, M., 665
Leight, Leonard, 886
Lema, Baltasar, 1118
Leslie, Eugene V., 888
Linder, William R., 1333
Ling, George M., 213
Ling, J. T., *854, 876, *1267
Ling, Ji-Toong, 886
Linnell, Folke, *673
Lister, James, 1331
Lofstrom, James E., *300
Lorber, John, 1101
Lott, J., 668
Louw, J. H., 1332
Love, Leon, *1193
Lubert, Mortimer, *767
Lubs, Herbert A., Jr., 442
Lucas, H. F., Jr., *1042
Lukes, Robert J., *944
Lundberg, George D., 1333
Lupien, Jules, 887

McAlister, William H., 1335
McAllister, R. G., *396
McCarty, Daniel J., Jr., *1248
McCaughey, William T. E., *83
McClintock, James T., 1332
McCullagh, E. Perry, 1116
McDonald, Eugene J., 443
McGaff, Charles J., 886
McMillan, John C., *571
McQueen, J. Donald, *336
McRae, D. L., 443

MacEwan, D. W., *37, 216, 1108
MacIntyre, R. S., 1107
Mackenzie, A. Ranald, *1016
Mahan, G. D., *386
Malagón Castro, Valentín, 217, 440
Malinow, Manuel René, 1118
Manfredi, O. L., *352
Marcarelli, Joseph L., *1059
Marchal, M., 443
Margaillan, A., 665
Margulis, Alexander R., *723, 1335
Marks, I. N., 1332
Marshak, Richard H., *709, *746
Marshall, Thomas R., *854, *1267
Martin, C. J., 1114
Martin, James F., *55
Martin, John A., *799
Martin, Mildred, 1109
Mathieson, Alister J. M., 888
Mattey, William E., *532
Maxwell, Morton H., 1106
Mead, Charles A., 1109
Meagher, Ronald P., 887
Melchior, J. C., 440
Melhem, Rafic E., *740
Melicow, Meyer M., *109, 1105
Menashe, Victor D., *571
Mertz, J. H. O., 1105
Meskin, Lawrence H., 442
Meyer, John S., *490
Meyer, Ralph R., *1208
Meyers, Phillip H., *1068
Millard, D. Glyn, *1231
Miller, C. E., *1042
Miller, Daniel G., *968
Miller, Roscoe E., 1334
Miyake, Tadashi, 1117
Moguilevsky, Jaime A., 1118
Montgomery, Max M., 1114
Moore, Booker T., *404
Moore, Thomas C., 211
Morrison, R. T., 670
Moss, William T., *294
Mudd, J. Gerard, *1287
Müller, H., 215
Mulvey, Bert E., 878
Murphy, John J., *1
Murray, Provan, *345
Murtagh, Frederick, *546
Mustard, Robert A., *978

Nelson, Sidney W., *445
Neuhauser, E. B. D., *63
Ney, Charles, *28, *72
Nezry, R., 443
Nice, Charles M., Jr., *1068
Nickson, James J., *938
Nicolò, A., 216
Nobler, Myron P., *522
Nogrady, M. B., *37
Norton, G. I., *756
Nourse, Myron H., 1105

O'Connor, G. A., 1108
O'Connor, J.-F., *63
O'Dell, James, 1330
O'Donnell, T. A., *1063
Olsen, Thomas G., 665
Ommaya, Ayub, K., *506
Opit, L. J., 1104
Overholt, E. L., 667

Pace, William R., Jr., 1114
Pajol, H., 441
Palmer, Eddy D., *774
Papatheodorou, Christos, 440
Pappas, Anthony, 1329
Parizel, G., 1329
Parker, R. G., *240
Parks, Raymond E., 1101
Pastremoli, A., 664
Patt, Harvey M., *928
Paus, Bernhard C., 1110
Payen, J., 664
Pelkey, W. J., 1113
Pellegrino, F., 441
Peracchia, G., 441
Perez-Tamayo, Ruheri, *1078
Peters, M. Vera, *956
Peterson, Harold O., 411
Pettit, Harold S., 1329
Phillips, Ralph F., *968, *1016
Philp, T., 1107, 1335
Pilz, Clifford G., 1114
Pircher, Felix J., 215
Pirson, Herbert S., *732
Pitman, R. G., 890
Platt, Melville A., 1103
Platten, Philip M., 1101
Podlaha, M., 219
Pohlit, Wolfgang, 672
Poppel, M. H., *727
Poppel, Maxwell H., *189
Poske, Robert M., 1114
Poutasse, J. David, *1333
Powell, P. R., 1113
Proudman, W. D., 1104
Pugh, David G., *1236
Pugh, R. C. B., 444
Pugsley, H. E., 885
Purzanski, W., 211

Quinn, James L., III, *135
Qvist, George, 886

Rabinowitz, Joseph L., 671
Rall, Kenneth L., *359
Ramsey, Elizabeth M., *638
Ray, Robert D., 671
Rayl, Donald F., 1101
Reveno, W. S., *735
Rhamy, Robert K., 1334
Richardson, Gene A., *1271
Richter, H., 1101
Riley, H. D., Jr., 1330
Riordan, Arthur F., 888
Roberts, Theophilus W., *89
Robicsek, Francis, 886
Rockoff, S. David, *506
Rogers, James V., Jr., *599
Roholt, Hartvig B., *159
Romieu, Cl., 441
Rominger, C. Jules, *835
Rose, John E., *403
Rose, Raymond G., *325
Rosen, Irving B., *978

Rosenbaum, H., *735
Rosenblum, David J., *1227
Rosin, Henry D., *1023
Rossmann, K., *178, *863
Routh, J. I., 670
Rowland, R. E., *1042
Rubenfeld, Sidney, *352
Rubin, S., *717
Russell, J. A., 665

Sachsse, Eckart, *792
Saltzstein, Sidney L., *723
Salvini, E., 1111
Salzman, Emanuel, 1332
Salzman, Ferdinand A., *373
Samuel, Eric, 1335
Sanders, A. P., *157
Sanders, Aaron P., *141
Sanger, Paul W., 886
Sansregret, André, *1156
Santín, Guillermo, 874
Sass, Martin, 1117
Sayegh, Emile S., 216
Scanlon, Paul W., *269, *280
Scatliff, James H., *823
Schanchs, Arthur F., 1106
Scharz, Joachim, 668
Schatzki, Richard, *805
Schauble, James F., 889
Scheer, Alan C., *939
Scheer, K. E., 214
Schencker, Bernard, *1059
Schmidt, Herbert W., 885
Schoenberg, Harry W., *1
Schreiber, Melvyn H., *1271
Schreiber, Richard R., 220
Schunk, H., 666
Schütterle, G., 214
Schwarz, Gerhart S., *109, 215
Sciebetta, M. Peter, *823
Scott, Michael, *546
Scott, Thomas F., 1108
Scott, Wendell G., 1305
Seaman, William B., *778, *859
Sears, A. D., *1205
Semat, Paul, 211
Seyler, Albert J., *1290
Shalek, Robert J., 1088
Shapiro, Bernard, 671
Shapiro, Jerome H., *522
Shapiro, Robert, *81, *578
Sharpe, Kathryn W., *141
Shuford, Wade H., *599
Siber, Ferris J., *373
Sieber, William K., 1114
Siffert, Robert S., 219
Sikov, Melvin R., *300
Silverstone, Sidney M., *1023
Simon, J. L., 1330
Sirota, Paul G., *325
Skaggs, Lester S., *221
Skillern, Penn G., 1116
Skinner, Norman S., 1309
Sklaroff, David M., *1052
Sky-Peck, Howard H., 671
Slim, Michael S., 1114
Smith, Robert T., 220
Smithers, D. W., 668
Snelling, Margaret D., *1032
Sokol, J. Kenneth, 214
Solomon, Nathan A., 1117
Soyka, D., 1101
Spjut, Harlan J., *97, *673, 1101
Spratt, John S., Jr., *673
Stasek, Vladimír, 672
Stein, Arthur H., Jr., 1110
Steinberg, Israel, *166, *528, *554
Steiner, R. E., 1329
Steinkamp, Ruth C., 672
Stephan, Günter, 671
Stephan, P., 443
Stiennon, O. Arthur, *811
Stifel, John L., 1310
Straube, Kurt R., 212, *571, *650, 1330
Sumerling, M. D., 1335
Swartz, Donald P., 1103

Taybi, H., 1330
Taylor, Frederick H., 886
Taylor, J. C., 665
Taylor, Samuel G., III, 671
Teich, Manfred, 672
Teng, Paul, 440
Texter, E. C., Jr., 887
Thibaudeau, Yvian, 671
Thomson, J. A., *345
Thomas, Lewis J., *506
Thomas, Martin A., 443
Thornbury, John R., *15, *1078
Tichy, Stanislav, 672
Till, J. E., *917
Tillotson, Peter M., *124
Toborowsky, Robert, *1
Tothill, P., 1107, 1107
Toye, D. K. M., 217
Trenckmann, H., 1101
Tristan, Theodore A., *1
Tsakiris, A., 441
Tucker, George L., *723
Turner, John W., *1167
Unger, Sol M., *189
Uson, Aurelio C., *109, 1105

Vallebona, D., 1109
Van Derstappen, G., 887
Van Itallie, Theodore B., *159
Van Ostrand, J. R., 1103
Van Velzer, D. A., 1107
Vasilas, Anthony, *844
Vezina, J. L., 443
Vidinli, M., 887
Vose, George P., 1112
Voutilainen, Antero, 669

Wachtler, Franz, 217
Walker, Lewis A., 1335
Walker, William A., *575
Wallace, E. N. K., 668
Wallace, Sidney, 212
Watson, John C., 1115
Watson, T. A., 1115
Webber, Milo, M., *26
Weens, H. Stephen, 1335
Wegst, Audrey V., 215
Weibel, Jorge, *1281
Weinberg, C. Richard, 1103
Weinstein, Aaron S., 1115
Welin, Solve, *673
Wellenbach, B., 1103
Wells, Josephine, *778, *859
Wells, L. H., 1109
Werbeloff, L., 1332
Westcott, Jack L., *554
Wetherbee, Donald G., *1167
Whitmore, Willet F., Jr., *1016
Wilcox, W. Curtis, *614
Williams, Bruce, 886
Williams, Hugh J., *1236
Williams, John Riley, *614
Willis, Theodore A., *1263
Willman, Vallee L., *1287
Wise, Robert E., *373
Wishard, W. Niles, Jr., 1105
Witten, David M., *115
Wohlgemuth, J., 1113
Wolf, Bernard S., *472, *709
Wood, Darrell D., *359
Wootton, P., *240
Wortzman, George, *462
Wray, James B., 1110

Youker, James, *673
Yunen, Jose R., *169

zum Winkel, K., 214
Zuppinger, A., 670

FOR YOUR FILES . . . Cut along this line

CONGENITAL HEART DISEASE: Septal defects

Congenital Heart Disease: Septal defects—2 CASES

CASE ONE: Ventricular septal defect: 17-year-old boy with infundibular stenosis

Patient had been free of symptoms. On physical examination a systolic murmur was present in the third and fourth left interspaces.

Electrocardiogram showed no evidence of ventricular hypertrophy.

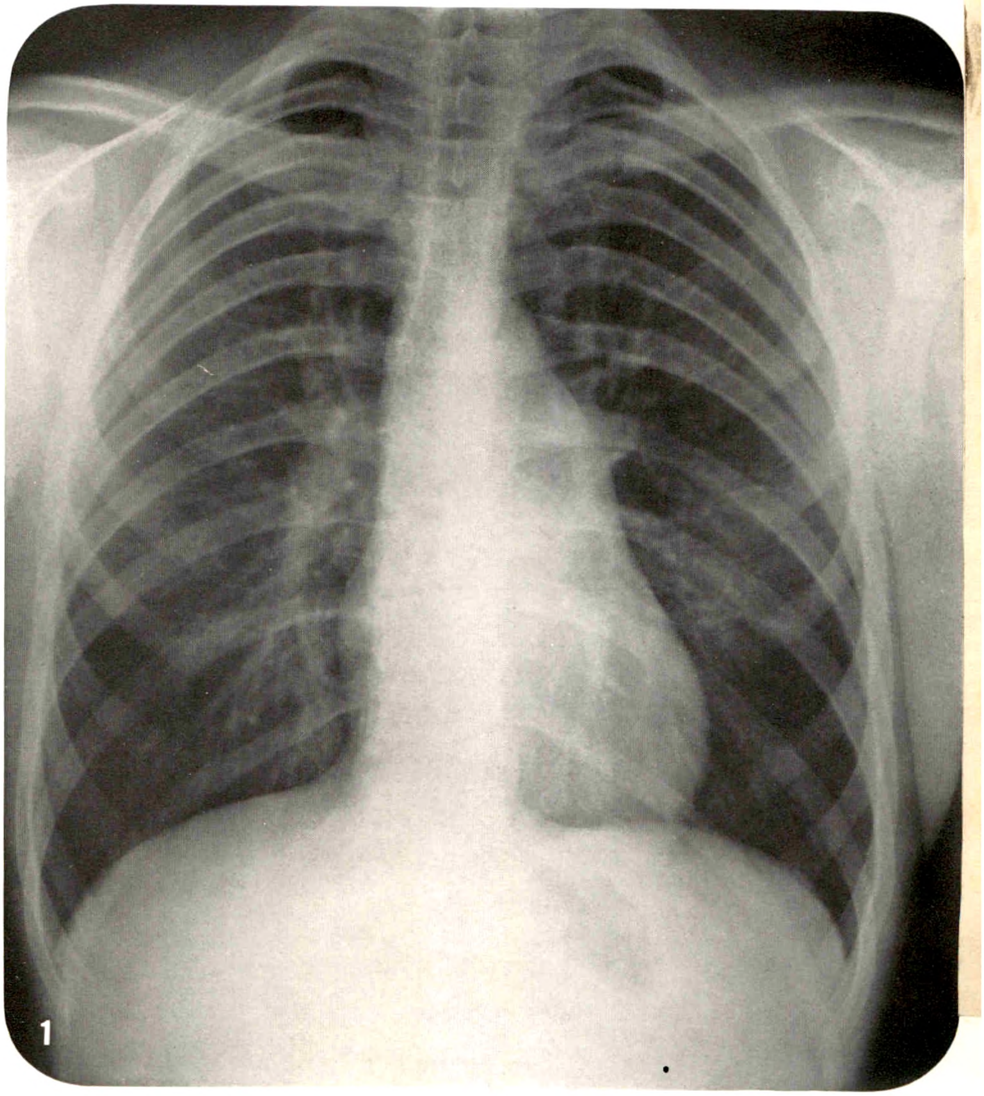


Figure 1. *Preoperative radiograph:* Note prominent main pulmonary artery.

CASE TWO: Atrial septal defect: Pulmonary stenosis in 27-year-old woman

For past year and a half patient has had progressive dyspnea on exertion with systolic murmur in the right area.

Radiograph (Figure 1) revealed enlargement of the right side of the heart. Cardiac catheterization demonstrated a right ventricular pressure of 210 mm Hg. and a small left-to-right shunt at atrial level.

At open heart surgery (Figures 2 and 3), a patent foramen ovale was closed and two additional small defects in the atrial septum were closed. A stenotic valve was opened. There was marked hypertrophy of the outflow tract of the right ventricle. No immediate fall in the right ventricular pressure followed surgery but postoperative course has been satisfactory.

Reprints available upon request. Write to address below stating quantity desired.

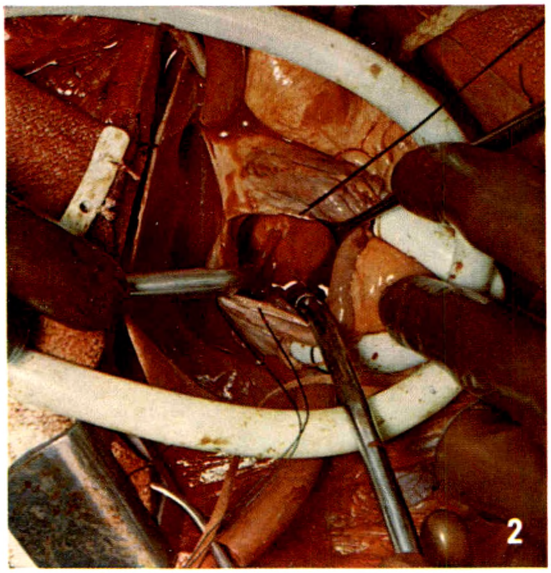


Figure 2. *Atriotomy* showing jet of blood spurting through small atrial septal defect.

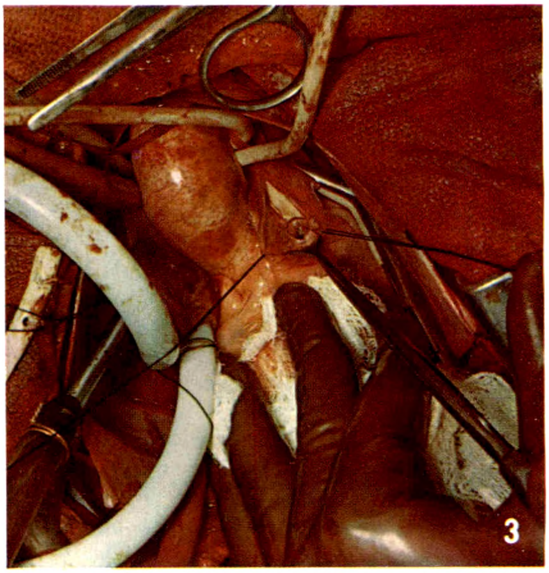


Figure 3. *Stenosed pulmonic valve* seen through opening in pulmonary artery.

Look to Kodak for medical x-ray film of highest quality—Kodak Royal Blue, Kodak's fastest medical x-ray film, and Kodak Blue Brand.

Look to Kodak for photographic film—color or black-and-white; also for Kodak color print materials.

Order KODAK x-ray products from your Kodak x-ray dealer
Order KODAK photographic products from your Kodak photographic dealer

X-ray Sales Division, EASTMAN KODAK COMPANY, Rochester 4, N.Y.

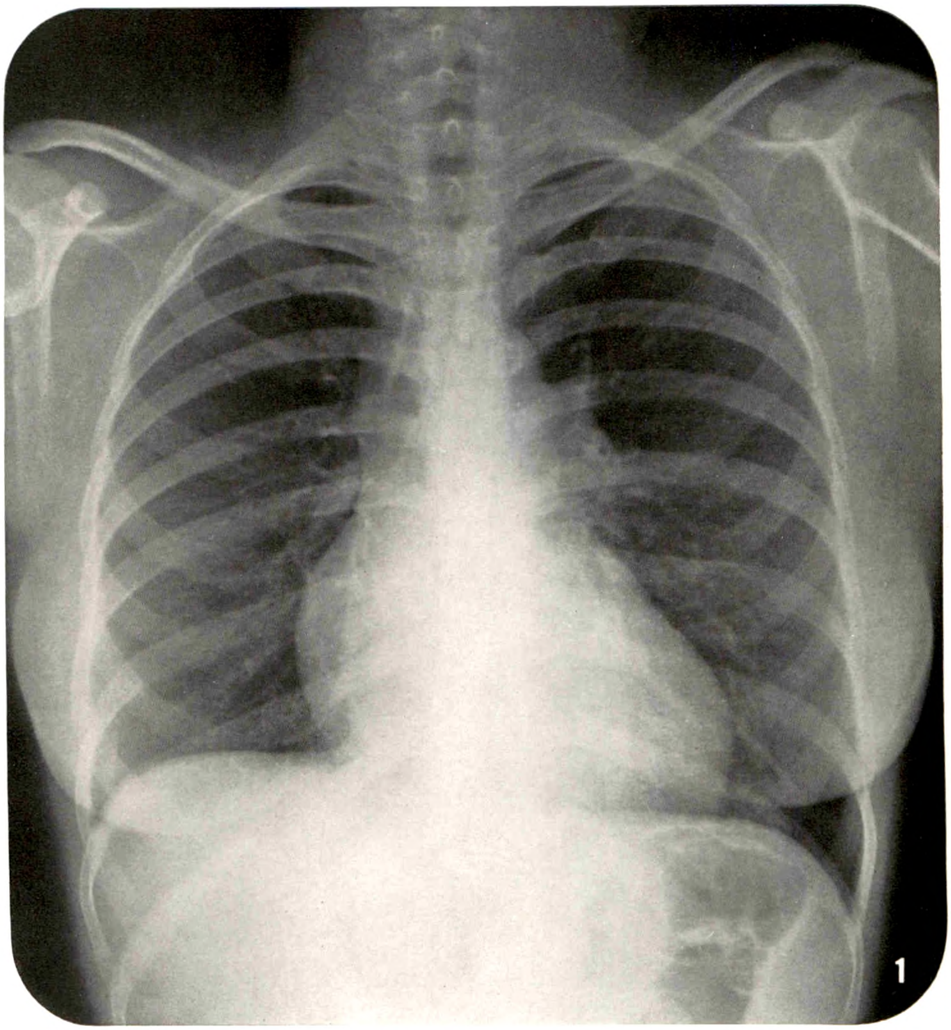


Figure 1. *Preoperative radiograph.* Note enlargement of right side of the heart.

HAVE A CAMERA HANDY loaded with KODAK film (color or black-and-white). With the KODAK RETINA Reflex III Camera, shown here, the physician is "master of every situation." A precision two-way photoelectric exposure control assures accurate settings. Choice of precision lenses available. What's more, the name RETINA includes a complete family of precision photo aids . . . specifically made for this camera to add extra scope and power.

Kodak
TRADEMARK

Radiograph (Figure 1) of heart showed only slight enlargement with prominent main pulmonary artery.

Cardiac catheterization revealed a ventricular septal defect and moderate infundibular pulmonic stenosis. At open heart surgery (Figures 2 and 3) a ventricular septal defect 1½ cm in diameter was closed and infundibulectomy was performed, eliminating the systolic gradient between the right ventricle and pulmonary artery.

Postoperative course has been satisfactory.

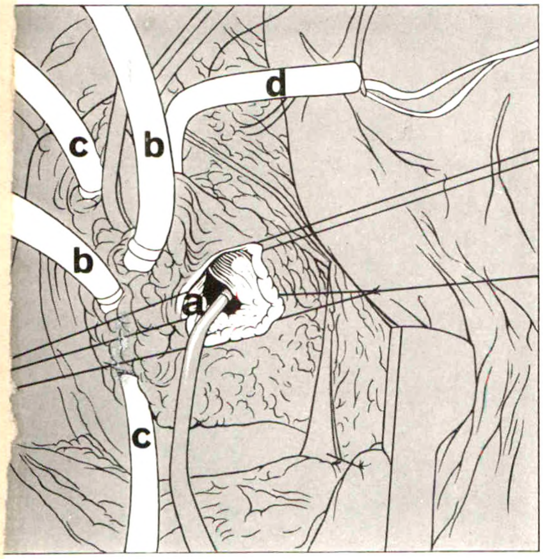
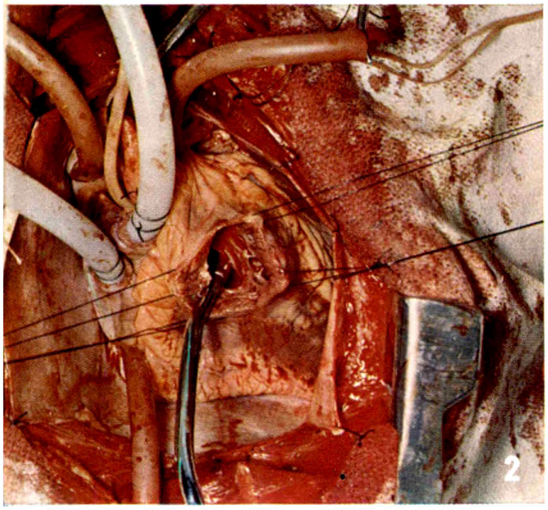
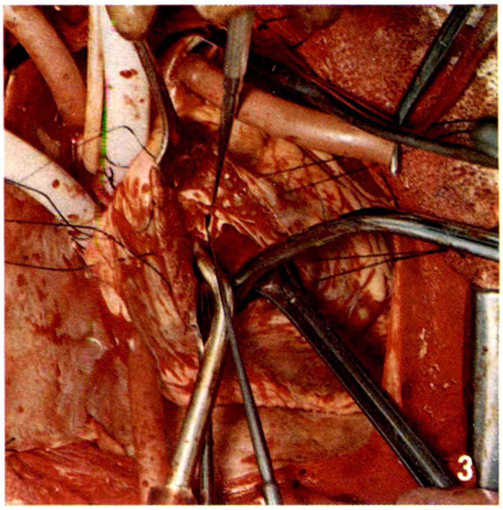


Figure 2. Note thickening of right ventricular muscle in outflow unit (infundibular stenosis).

DIAGRAM for Figure 2 to show essential morphological features: **a.** Right ventriculotomy showing infundibular hypertrophy; **b.** Venae cavae drainage tubes; **c.** Snares around cavae; **d.** Snare around pulmonary artery.

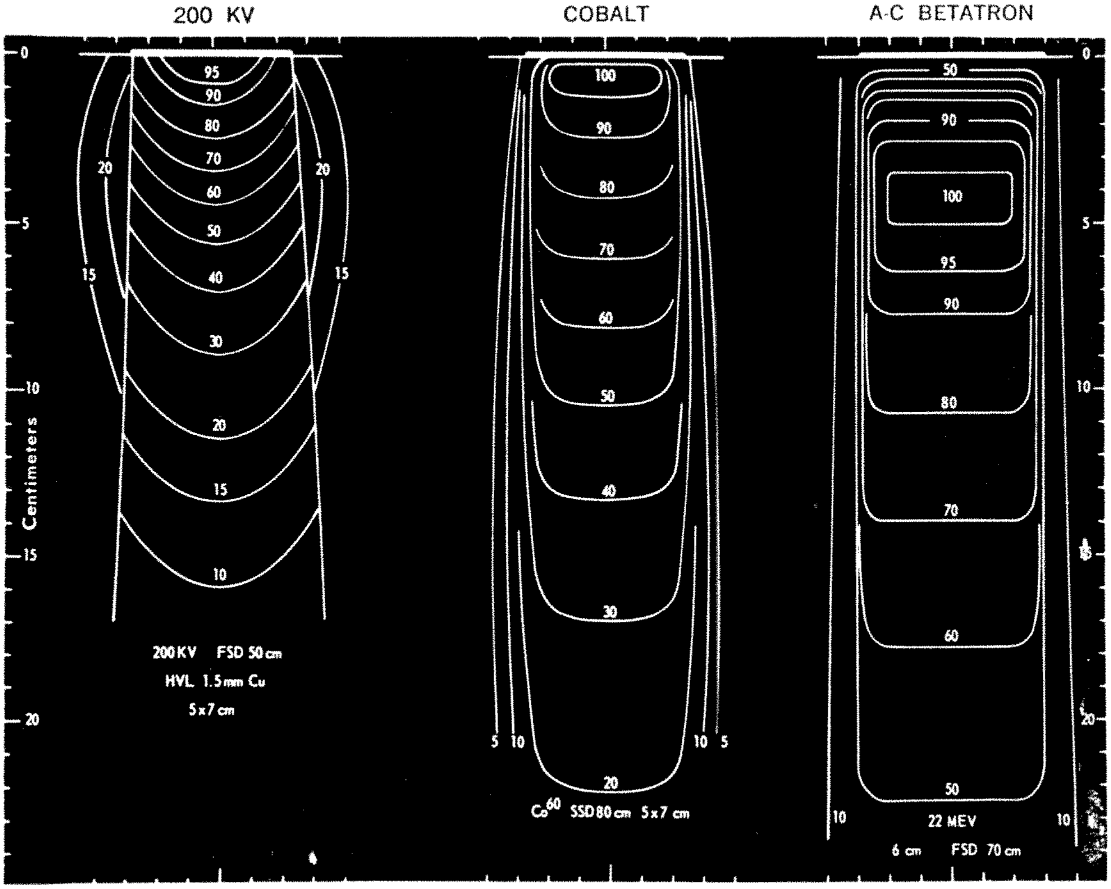
Figure 3. *Defect* with nerve hook at each end.


2


3

FOR DETAILS OF CASE TWO—TURN PAGE.

COMPARISON of ISODOSE CURVES for 200 KV, COBALT and BETATRON RADIATION



ALLIS-CHALMERS
TWENTY-FIVE MILLION VOLT
BETATRON

30-50% MORE TUMOR DOSE
45-50% LESS ENTRANCE DOSE

You treat deep tumors with less damage to intervening tissue with the Allis-Chalmers 25 Mev Betatron. As shown above, this high-energy, high intensity equipment, operating at 22 Mev, delivers 50% of dose to the surface — *70% of dose* at almost 15 centimeters down. Treatment is accomplished with fewer applications.

Less discomfort to the patient. With a focal spot of only 0.2mm, there is a complete absence of side-scattered radiation — penumbra is absent. Precise aiming of the beam puts the radiation exactly where you want it . . . adjoining tissue is unaffected.

You simplify treatment. Rotational therapy is unnecessary with the Allis-Chalmers Betatron. You need calculate only one readily-delineated portal. With the highest ratio of tumor dose to total body dose, the Allis-Chalmers Betatron eliminates the need for complex therapy planning.

Allis-Chalmers Betatrons have been proving their economy, reliability and effectiveness in medicine, research and industry since 1944. You're assured dependable operation.

• • •

Examine 25 Mev therapy. See your nearest A-C representative, or write Allis-Chalmers, Accelerator Department, Milwaukee 1, Wis.

ALLIS-CHALMERS

A-1742

Just out

THE SALIVARY GLANDS IN RADIOLOGICAL DIAGNOSIS

By* GIAN FRANCO GARUSI, *Bologna

VIII + 160 p., 153 fig., 1964. US $10.10
(Bibliotheca Radiologica, Fasc. 4)

Contents

Foreword by Prof. G. TORI

I. Anatomy
II. Physiology
III. Sialographic Technique
IV. Normal Sialographic Aspects and their Variations
V. Increase in Volume of the Major Salivary Glands, with or without Functional Changes
VI. Congenital Alterations of the Major Salivary Glands
VII. Phlogistic Processes of the Parotid and Submandibular Salivary Glands
VIII. Calculous Conditions of the Major Salivary Glands
IX. Tumors of the Parotid and Submandibular Salivary Glands
X. Imprints and Displacements of the Salivary Glands from Extrinsic Causes
XI. Angiomas of the Cheek and the Submandibular Region
XII. Sialography in Bone Tumors of the Mandible
XIII. Alterations of the Major Salivary Glands from Ionizing Radiations
XIV. Rare Affections of the Major Salivary Glands
XV. The Sublingual Salivary Glands
XVI. Conclusions
XVII. References

Please write for index of Fasc. 1—4 of this series

S. KARGER AG, Arnold-Böcklin-Strasse 25, BASEL (Switzerland)

Please send me: ....

Name ....

Address ....

Please place your order with:

Albert J. PHIEBIG, P.O. Box 352, White Plains, N. Y.